MERRIMACK PHARMACEUTICALS INC
Form 10-K
March 06, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

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

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number 001-35409

Merrimack Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	04-3210530
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
One Kendall Square, Suite B7201	
Cambridge, MA	02139
(Address of principal executive offices)	(Zip Code)

Registrant’s telephone number, including area code: (617) 441-1000

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

Title of each class	Name of each exchange on which registered
Common Stock, $0.01 par value	Nasdaq Global Market

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

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

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

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K 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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the last sale price for such stock on June 29, 2018, was $62,302,160.

As of February 27, 2019, there were 13,342,784 shares of Common Stock, $0.01 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A in connection with its 2019 Annual Meeting of Stockholders. Portions of such proxy statement are incorporated by reference into Part III of this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "c expressions are intended to identify forward looking statements, although not all forward looking statements contain these identifying words.

The forward looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- our plans to develop and commercialize our product candidates and diagnostics;
- our ongoing and planned discovery programs, preclinical studies and clinical trials;
- the timing of the completion of our clinical trials and the availability of results from such trials;
- the anticipated cost savings in connection with our restructuring efforts;
- our plans to explore strategic alternatives;
- our ability to establish and maintain collaborations for our product candidates;
- our receipt of payments related to the milestone events under the asset purchase and sale agreement with Ipsen S.A. or under the license and collaboration agreement between Ipsen S.A. and Les Laboratoires Servier SAS (as assignee from Shire plc), when expected or at all;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of our product candidates;
- our intellectual property position;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the potential advantages of our approach to drug research and development; and
- our estimates regarding expenses, future revenues, capital requirements and needs for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in Part I, Item 1A. Risk Factors, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures, collaborations or investments that we may make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

NOTE REGARDING TRADEMARKS

ONIVYDE® is a registered trademark of Ipsen S.A. Any other trademarks, trade names and service marks referred to in this Annual Report on Form 10-K are the property of their respective owners.

PART I

Item 1. Business

Overview

We are a clinical stage biopharmaceutical company based in Cambridge, Massachusetts that is outthinking cancer by targeting biomarker-defined cancers. Our vision is to ensure that cancer patients and their families live fulfilling lives. Our mission is to transform cancer care through the smart design and development of targeted solutions based on a deep understanding of cancer pathways and biological markers. Our strategy is to (1) understand the biological problems we are trying to solve, (2) design specific solutions against the problems we are trying to solve and (3) develop those solutions for biomarker-selected patients. This three-pronged strategy seeks to ensure optimal patient outcomes. We own worldwide development and commercial rights to all of our clinical and preclinical programs.

Our only clinical stage asset in active development is MM-310. MM-310 is an antibody-directed nanotherapeutic that targets the ephrin receptor A2, or EphA2, receptor and contains a novel cytotoxic taxane. The EphA2 receptor is highly expressed in most solid tumor types, such as prostate, ovarian, bladder, gastric, pancreatic and lung cancers. We are conducting a Phase 1 clinical trial to evaluate safety and preliminary activity of MM-310 in patients with solid tumors and to identify the maximum tolerated dose.

Our two most promising preclinical programs are MM-401, an agonistic antibody targeting a novel immuno-oncology target, TNFR2, and MM-201, a highly stabilized agonist-Fc fusion protein targeting death receptors 4 and 5.

On June 25, 2018, we announced top-line results from our global, double-blinded, placebo-controlled, Phase 2 randomized CARRIE clinical trial evaluating the addition of MM-141 (istiratumab) to standard-of-care treatment in patients with previously untreated metastatic pancreatic cancer and high serum levels of the insulin-like growth factor 1, or IGF-1. The CARRIE clinical trial did not meet its primary or secondary efficacy endpoints in patients who received MM-141 in combination with nab-paclitaxel and gemcitabine, compared to nab-paclitaxel and gemcitabine alone. These results were consistent in all subgroups analyzed. Based on these results, we are not devoting additional resources to and have ceased all of our development activities for MM-141.

On October 19, 2018, we announced the termination of our global, open-label, biomarker-selected, Phase 2 randomized SHERLOC clinical trial evaluating MM-121 (seribantumab) in combination with docetaxel in patients with heregulin positive non-small cell lung cancer, or NSCLC. The decision to terminate the SHERLOC clinical trial was made based on an interim analysis triggered by the occurrence of 75% of events required for trial completion, which demonstrated that the addition of MM-121 to docetaxel did not improve progression free survival over docetaxel alone in this patient population.

On November 7, 2018, based on the results of the interim analysis of the randomized Phase 2 SHERLOC clinical trial that were announced on October 19, 2018, we announced that we are discontinuing development of all ongoing MM-121 programs, including terminating the global, double-blinded, placebo-controlled, biomarker-selected, Phase 2 randomized SHERBOC clinical trial evaluating MM-121 in combination with fulvestrant in patients with heregulin positive, hormone receptor positive, ErbB2 (HER2) negative, metastatic breast cancer.

On November 7, 2018, we also announced that we were implementing a reduction in headcount as part of a corporate restructuring, after which we expected to have approximately 27 employees. The corporate restructuring followed a comprehensive review of our drug candidate pipeline. The reduction in headcount was completed in February 2019.

In connection with the corporate restructuring, we also announced on November 7, 2018 that we have retained external advisors to explore strategic alternatives.

On April 3, 2017, we completed the sale, or the asset sale, to Ipsen S.A., or Ipsen, of our right, title and interest in the non-cash assets, equipment, inventory, contracts and intellectual property primarily related to or used in our business operations and activities involving or relating to developing, manufacturing and commercializing ONIVYDE, our first commercial product, and MM-436, or the commercial business. Our non-commercial assets, including our clinical and preclinical development programs described above, or the pipeline business, were not included in the asset sale and remain assets of ours.

Our Approach to Cancer Research

We are executing a three-pronged strategy as the basis for our approach to drug development. Our process begins with identifying the problems we are trying to solve and developing a fundamental understanding of how cancer cell signaling pathways and drug metabolism affect those problems. We then engineer product candidates, which include both antibodies and antibody-directed nanotherapeutics, which are designed to match the problem and fit our understanding of the target. Finally, we test our product candidates in biomarker-defined populations that are more homogenous than the general unselected disease population. This strategy improves our ability to detect a clear signal early in clinical development and enables us to pursue smaller, shorter, more personalized studies with lower development costs and a potentially accelerated timeframe to clinically meaningful data.

Step 1: Understand the problem

To understand the problems we are trying to solve, we begin by developing a deep understanding of how cancer pathways and drug metabolism affect those problems. Using systems biology and systems pharmacology, our goal is to understand how the complex molecular interactions that occur within cell signaling pathways, or networks, lead to cancer. Our approach utilizes proprietary, dynamic biological data generated in a high-throughput method in which we test multiple biological or chemical parameters using engineering, analytical and modeling expertise, and from which we build computational models of cell biology to further our drug discovery, design and predictive development. We have developed an expertise in generating kinetic data, describing molecular changes or interactions over time, to illuminate the dynamic interactions that occur within biological systems. We apply those insights throughout the research and development process, including for target identification, lead compound design and optimization, diagnostic discovery and the design of clinical trial protocols.

Our models are constructed and validated using internally generated and proprietary data sets. Following the validation of a comprehensive model of a cell signaling network, we are able to use the model for drug discovery. A significant portion of our discovery work takes place in silico, or using the model for computer simulation, which we believe is a more efficient and productive approach for drug discovery and development than traditional approaches.

Step 2: Design a specific solution

Once we understand the problem that we are trying to solve and have developed a clear target, we design a very specific solution to fit our deep understanding of the target, using two internal platforms: our engineered antibody platform and our antibody-directed nanotherapeutics platform.

Human monoclonal antibodies

Human antibodies are a key component of many of our targeted therapies based on a range of favorable attributes, including significant target specificity and avidity relative to small molecules and well-understood pharmacokinetic properties. Our human monoclonal antibody engineering platform provides us with the ability to create antibodies that are designed to inhibit specific nodes responsible for tumor growth and survival, or to address inherent drug resistance by simultaneously targeting redundant signaling pathways. We have designed antibodies both for use as stand-alone therapeutics and as targeting or docking agents for our antibody-directed nanotherapeutics. We have worked with several antibody formats, including:

- fully human recombinant monoclonal antibodies and fragments of fully human recombinant monoclonal antibodies that include the antibody binding domain. Monoclonal antibodies and antibody fragments are proteins that bind specifically to one defined site on a cell surface protein or receptor;
- stabilized ligand-fusions, either alone or in a bispecific targeted format with an antibody domain;
- multi-specific antibody formats, which are comprised of two or more antibodies or antibody fragments linked to a common scaffold molecule to produce a single molecule that binds to distinct epitopes on two or more target cell surface proteins or receptors; and
- oligoclonal antibody mixtures, which are comprised of defined ratios of two or more recombinant human monoclonal antibodies that target two or more distinct epitopes on a single cell surface protein or receptor.

Antibody-directed nanotherapeutics

Our antibody-directed nanotherapeutics platform is a next-generation antibody drug conjugate, or ADC, that enables us to create actively targeted liposomes that can contain different chemotherapeutic agents. Our targeted nanotherapeutics are lipidic particles constructed to stably encapsulate active drug payloads. Nanoscale objects typically, though not exclusively, have dimensions on the order of 100 nanometers or smaller. We believe that our

nanotherapeutics offer the following potentially favorable attributes:

- a multi-layered targeting strategy that includes an antibody targeting ligand against a preferentially expressed cell-surface receptor on tumor cells, size-controlled accessibility to the tumor microenvironment but not to most normal tissues, and a selective active payload for delivery;
- a uniform nanoscale size, which is intended to enable targeting and preferential deposition within tumors by taking advantage of the enhanced permeability and retention effect to selectively enter, and subsequently accumulate in, tumors with leaky vasculature;
- a formulation designed to minimize the leakage of active drug payload out of the particle before the nanotherapeutic has reached the tumor, with the goal of limiting systemic exposure and the associated occurrence of adverse events, while maximizing the amount of active drug that reaches the target;

- encapsulation of small molecules or nucleic acids in lipidic nanoparticles, designed to protect the active drug payload as it passes through the circulation and organs of the body, such as the liver, and to prevent premature clearance or metabolism of the active drug, and thereby extend the pharmacokinetic profile and enable more convenient dosing regimens; and
- a customizable payload by which our nanotherapeutics can contain a variety of drug payloads, including chemotherapies, cytotoxics, molecularly targeted small molecule drugs, and nucleic acids, such as siRNA and genes. Unlike conventional ADCs, our antibody-directed nanotherapeutics do not require the use of ultra-high potency drugs or direct conjugation to the antibody, both of which can constitute considerable limitations to the conventional ADC platform.

Step 3: Test the solution in a homogenous patient population

With a clear understanding of the problem and a custom-designed solution, we target our product candidates to biomarker-defined populations. Every program must utilize a biomarker signature, and accordingly our companion diagnostics are being designed to test for such biomarkers and thereby provide prognostic and predictive value for enrichment of the patient populations. Utilizing companion diagnostics to identify the biomarker-defined population, our clinical trials are designed to test our product candidates in more homogenous patient populations.

Ultimately, we believe that our approach will result in better treatments for complex diseases by incorporating the identification of biomarkers and the development of associated companion diagnostics into the drug development process. We believe this may enable physicians to better deliver the right drug to the right set of patients at the right time, which may in turn improve patient outcomes, reduce the overall costs of treating and caring for cancer patients, and ultimately may provide a basis for seeking favorable reimbursement of approved drugs from payors.

Our Product Candidates

MM-310

MM-310 overview

MM-310 is an antibody-directed nanotherapeutic that encapsulates a newly engineered form of the highly potent chemotherapy docetaxel as a prodrug in an EphA2 targeted liposome. In preclinical studies, MM-310 demonstrated increased antitumor activity in multiple models compared to free docetaxel. In the preclinical studies, EphA2-targeted liposomes delivered the cytotoxic to the tumor while minimizing exposure to healthy tissues. MM-310 is designed to result in prolonged exposure of the active drug at the tumor site and in preclinical studies had a significantly longer half-life than free docetaxel. In a sampling of approximately 200 tumors, EphA2 was found to be expressed in tumor cells, myofibroblasts and/or tumor-associated blood vessels. EphA2 overall prevalence was found to range from 50% to 100% across multiple indications. In cell models, a high level of specificity was observed in the MM-310 EphA2 targeted liposome, with a more than 100-fold increase in liposome cell association when compared to non-targeted liposomes. MM-310 is not approved for any indication by the U.S. Food and Drug Administration, or FDA, or any other regulatory agency.

Our three-pronged drug development strategy informs our approach to our MM-310 program:

Understand the problem. Conventional ADCs, which typically incorporate an ultra-high potency drug conjugated to a targeting antibody and which do not utilize liposomes to encapsulate the payload, can be highly effective therapies but are often accompanied by significant toxicities that limit tolerable dosage levels and duration of use. Other potential limitations of conventional ADCs include the need for direct conjugation of the drug to the antibody, which requires subsequent cleavage of the bond to release the drug, and the uptake of the conventional ADC into normal tissue due to both the small size of the ADC and the presence of the accessible target receptor on normal tissue. Docetaxel, the

payload for MM-310, is a highly effective and well validated cancer chemotherapy with a conventional potency range, but it is often accompanied by significant toxicity that limits its dosage levels and duration of use. Our hypothesis is that a more sustained release of the drug should result in lower plasma levels and extended exposure at the tumor, and thus less toxicity and improved efficacy. We also believe that EphA2 is an attractive target due to the fact that it is expressed at a very high level on and internalized by cancer cells.

Design a specific solution. MM-310 is an antibody-directed nanotherapeutic that is designed to improve the therapeutic window of the active drug by incorporating it in the form of a drug precursor encapsulated in a nanoliposome to ensure a slower and more sustained release of the drug. The small size of the nanotherapeutic may allow it to take advantage of the leaky vasculature of the tumor through the permeability and retention effect and potentially deliver docetaxel more preferentially, while restricting distribution in normal tissues. The nanoliposome utilizes antibodies to the EphA2 receptor, a receptor often over-expressed in solid tumors, to help target more of the chemotherapy payload to the tumor site.

Test the solution in a homogenous patient population. After identifying the maximum tolerated dose and the drug's safety profile in humans, future clinical trials will test the drug in tumor types that over-express the EphA2 receptors.

MM-310 Phase 1 clinical trial

In March 2017, we initiated a Phase 1 clinical trial of MM-310 to evaluate its safety and preliminary activity in patients with solid tumors and to identify the maximum tolerated dose. Although early data from the clinical trial from the every three week dosing schedule regimen showed signs of encouraging antitumor activity in four patients, emerging cumulative grade 3 peripheral neuropathy following multiple cycles of treatment was observed in three patients. Pharmacokinetic and preclinical data indicate that lengthening the time between dosing may improve the tolerability of MM-310. As a result, on November 7, 2018, we announced an amendment to the clinical trial to extend the dosing interval of MM-310 from every three weeks to every four weeks.

On March 6, 2019, we provided an update regarding the patients dosed on the amended protocol, noting that three patients have been enrolled in the 360 mg every four weeks dose cohort under the amended protocol, which matches the highest dose level reached during the prior version of the protocol at every three weeks. As of March 4, 2019, all three patients in the 360 mg every four weeks dose cohort continued to be treated in the study: one patient had completed 98 days of treatment and received four cycles of MM-310, reaching stable disease as a best response to date; the second patient had completed 56 days of treatment and received two cycles of MM-310; and the third patient received the first dose 21 days prior. Importantly, no instances of grade 3 peripheral neuropathy were reported in this cohort. If all three patients in the 360 mg every four weeks dose cohort successfully complete the observation period for dose-limiting toxicities, which is expected to occur in mid-March, we would plan to begin enrolling the next dose-escalation cohort at 420 mg of MM-310 every four weeks.

MM-310 diagnostic development

We utilize a validated test to retrospectively evaluate patients for EphA2 receptor expression in our ongoing Phase 1 clinical trial of MM-310.

Preclinical Product Candidates

We are developing preclinical product candidates for a range of solid tumor indications. Our two most promising preclinical programs are MM-401, an agonistic antibody targeting a novel immuno-oncology target, TNFR2, and MM-201, a highly stabilized agonist-Fc fusion protein targeting death receptors 4 and 5.

CARRIE, SHERLOC and SHERBOC Clinical Trials

We have discontinued development of our MM-121 and MM-141 product candidates based on results from our CARRIE, SHERLOC and SHERBOC clinical trials of such candidates.

MM-121 (seribantumab)

MM-121 is a fully human monoclonal antibody that targets ErbB3 (HER3), a cell surface receptor that is activated by its ligand heregulin. Heregulin-driven ErbB3 (HER3) signaling has been implicated as a mechanism of tumor growth and broad resistance to cytotoxic, anti-endocrine, targeted and immuno-oncology therapies. When used in combination with anti-cancer drugs, MM-121 is designed to block heregulin-driven ErbB3 (HER3) signaling and enhance the anti-tumor effect of combination therapy partners.

In February 2015, we initiated the global, open-label, biomarker-selected, Phase 2 randomized SHERLOC clinical trial evaluating MM-121 in combination with docetaxel, versus docetaxel alone, in patients with heregulin positive NSCLC. On October 19, 2018, we announced the termination of the SHERLOC clinical trial based on an interim analysis triggered by the occurrence of 75% of events required for trial completion, which demonstrated that the

addition of MM-121 to docetaxel did not improve progression free survival over docetaxel alone in this patient population.

In February 2018, we dosed the first patient in our global, double-blinded, placebo-controlled, biomarker-selected Phase 2 randomized SHERBOC clinical trial evaluating MM-121 in combination with fulvestrant, versus fulvestrant alone, in patients with heregulin positive, hormone receptor positive, ErbB2 (HER2) negative, metastatic breast cancer. On November 7, 2018, we announced that we are discontinuing development of all ongoing MM-121 programs, including terminating the SHERBOC clinical trial based on the results of the interim analysis of the SHERLOC clinical trial.

We previously evaluated MM-121 in multiple Phase 1 and Phase 2 clinical trials in combination with both chemotherapies and other targeted agents across a wide spectrum of solid tumor patient populations, including patients with ovarian, breast and lung cancers. Over 700 patients were treated with MM-121 in those previous clinical trials. The goal of these clinical trials was to explore the efficacy and safety of MM-121 in combination with other agents and to establish and validate clinically meaningful biomarkers to identify patients most likely to benefit from MM-121.

MM-141

MM-141 is a fully human tetravalent bispecific antibody designed to block tumor survival signals by targeting receptor complexes containing the insulin-like growth factor 1 receptor, or IGF-1R, and ErbB3 (HER3) cell surface receptors. A tetravalent bispecific antibody is a single molecule that has four binding sites, two for each of two different target cell surface receptors. IGF-1R and ErbB3 (HER3) both activate a major signaling pathway, PI3K/AKT/mTOR, that allows tumor cells to grow and develop resistance to chemotherapy. We designed MM-141 to suppress the PI3K/AKT/mTOR signaling pathway by reducing the levels of IGF-1R and ErbB3 (HER3) that trigger the pathway.

In May 2015, we initiated the global, double-blinded, placebo-controlled, Phase 2 randomized CARRIE clinical trial evaluating MM-141 in combination with nab-paclitaxel and gemcitabine, versus nab-paclitaxel and gemcitabine alone, in patients with previously untreated metastatic pancreatic cancer with high serum levels of free insulin-like growth factor 1, or IGF-1. In June 2018, we announced top-line results from the CARRIE clinical trial, showing that the trial did not meet its primary or secondary efficacy endpoints in patients who received MM-141 in combination with nab-paclitaxel and gemcitabine, compared to nab-paclitaxel and gemcitabine alone. These results were consistent in all subgroups analyzed. Based on these results, we are not devoting additional resources to and have ceased all of our development activities for MM-141.

Manufacturing

We do not have any manufacturing facilities or personnel. We have relied on contract manufacturing organizations to manufacture our product candidates in order to meet our operational objectives for clinical testing, as well as for commercial manufacture if our product candidates receive marketing approval. We have also outsourced all fill finish, packaging, labeling and distribution activities. We are not currently planning to manufacture bulk product for any of our product candidates in 2019.

We do not currently have manufacturing arrangements in place for our active product candidates. To the extent we advance any product candidates, we expect that we would identify and qualify manufacturers to provide the active pharmaceutical ingredient and fill finish services as a part of such development.

We are identifying, developing and testing diagnostic assays for predictive biomarkers in an internal laboratory and through collaborations with third-parties. Upon completion of the development of the diagnostic tests, we plan to evaluate external as well as internal options for manufacturing and commercialization of the tests.

Sources and Availability of Raw Materials

We currently rely on single source suppliers for certain raw materials that we use for our antibody and nanoliposome manufacturing processes. We purchase these materials from our suppliers on a purchase order basis and do not have long-term supply agreements in place.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our integrated research, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. 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 resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products 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. 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. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of 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, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours. In addition, our ability to compete may be affected because in many cases insurers or other third-party payors seek to encourage the use of generic products. There are many generic products currently on the market for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

The initial focus of our business is to develop therapeutics and diagnostics for the treatment of solid tumor cancers. Cancer is the second most common cause of death in the United States, exceeded only by heart disease. There are a variety of available drug therapies marketed for solid tumors. Although there has been considerable progress over the past few decades in the treatment of solid tumors and the currently marketed therapies provide benefits to many patients, generally these therapies all are limited to some extent in their efficacy and frequency of adverse events, and none of them are successful in treating all patients. As a result, the level of morbidity and mortality from solid tumor cancers remains high. In many cases, these drugs are administered in combination to enhance efficacy. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors.

In addition to any marketed therapies for solid tumors, there are a number of products in late stage clinical development to treat solid tumors. These products in development may provide efficacy, safety, 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.

The following table sets forth information about certain solid tumor cancer indications that are eligible for inclusion in our Phase 1 clinical trial of MM-310. The U.S. estimated annual incidence is based on information from the American Cancer Society, Cancer Fact & Figures 2019.

Tumor Type	U.S. Annual Incidence
Lung and bronchus	228,150
Bladder	80,470
Endometrial	61,880
Pancreatic	56,770
Gastric	55,750
Ovarian	22,530
Sarcomas (soft tissue)	12,750

Collaboration and License Agreements

We are party to certain collaboration and license agreements. We consider the following agreements to be material to our business.

Ipsen

On April 3, 2017, we completed the asset sale with Ipsen. Pursuant to the Asset Purchase and Sale Agreement, dated as of January 7, 2017, or the asset sale agreement, between us and Ipsen, Ipsen acquired our right, title and interest in the commercial business. Pursuant to the asset sale agreement, we received $575.0 million in cash, plus a working capital adjustment of $5.7 million, and are eligible to receive up to $450.0 million in additional regulatory approval-based milestone payments. Ipsen has agreed pursuant to the asset sale agreement to use commercially reasonable efforts to develop ONIVYDE in connection with obtaining the regulatory approval by the FDA of ONIVYDE for certain indications. We also retained the right to receive net milestone payments that may become payable for the ex-U.S. development and commercialization of ONIVYDE for up to $33.0 million pursuant to a license and collaboration agreement between Ipsen and Les Laboratoires Servier SAS, or Servier (as assignee from Shire plc), which we refer to as the Servier agreement. To date, we have received $28.0 million of the potential $33.0 million in milestone payments under the Servier agreement. We entered into the Servier agreement in 2014, and on April 3, 2017, the Servier agreement was assigned to Ipsen in connection with the completion of the sale of the commercial business.

In connection with the asset sale, we entered into a sublease agreement with Ipsen under which Ipsen is subleasing approximately 64,550 square feet of our leased space in Cambridge, Massachusetts through the end of our lease term on June 30, 2019.

Intellectual Property

Our success will significantly depend on our ability to obtain and maintain patent and other proprietary protection for our commercially important technology, inventions and know-how, defend and enforce our patents, preserve the confidentiality of our trade secrets, establish and protect our commercial brands and operate without infringing the valid and enforceable patents and proprietary rights of third parties. To accomplish this, we rely on a combination of intellectual property rights, including patents, trade secrets, copyrights and trademarks, as well as regulatory exclusivity and contractual protections. We aggressively strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover our products and compositions, their methods of use and processes for their manufacture, as well as our diagnostic and drug discovery technologies and any other inventions that are commercially important to the development of our business. In some circumstances, 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, such as our proprietary network modeling programs and large scale protein and liposome production methods.

We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and contractors. We require each of our employees, consultants and advisors to execute a confidentiality and inventions assignment agreement before beginning their employment, consulting or advisory relationship with us. These agreements generally provide that the individual must keep confidential and not disclose to other parties any confidential information developed or learned by the individual during the course of their relationship with us except in limited circumstances. These agreements also generally provide that we will own all inventions conceived by the individual in the course of rendering services to us. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection of the use, formulation, manufacture and composition of our products and product candidates, as well as successfully asserting and/or defending these patents against third-party challenges. Our ability to protect our products and product candidates from unauthorized making, using, selling, offering to sell or importing by third parties is dependent on the extent to which we have rights under valid and enforceable patents that cover these activities.

As of January 31, 2019, we owned or controlled a total of 15 issued U.S. patents and 121 corresponding issued foreign patents, in addition to 25 pending U.S. patent applications and 113 pending patent applications in the rest of the world. We intend to continue to protect our proprietary technology with additional filings as appropriate. We do not have patents or patent applications in every jurisdiction where there is a potential commercial market for our product candidates. We continually evaluate our patent portfolio and patent strategy and believe our owned and licensed patents and patent applications, as well as applicable periods of regulatory exclusivity available after new product approval, provide us with a competitive advantage; however, if markets where we do not have patents or patent applications become commercially important, our business may be adversely affected.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application.

In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each drug and other factors, including those involved in the filing of a new drug application, or NDA, or a biologics license application, or BLA. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process, provided the total 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 calculated as one-half the time between the effective date of an investigational new drug application, or IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the FDA's approval of that application. Only one patent applicable to each approved drug is eligible for the extension and the application for extension must be made prior to expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration.

Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. The stated patent exclusivity dates for patent exclusivity outside of the United States may also be eligible for further extension, and/or regulatory market and/or data exclusivity in certain countries, upon product approval in individual countries for various reasons, including supplemental protection certificate(s) after product approval in eligible countries outside the United States, and/or conducting certain investigations of pediatric exclusivity or use of products covered by the applicable patent.

MM-310

We have an exclusive license to pending patent applications covering the MM-310 composition through at least 2037 (if issued) from the University of California. In addition, we own multiple pending patent applications covering the MM-310 liposome composition, companion diagnostic technology for MM-310 and therapeutic uses of MM-310 through at least 2037 (if issued). Our latest-expiring granted patent covering the composition or use of MM-310 in the United States will expire in 2031, and the latest-expiring granted patent covering MM-310 in one or more countries outside the United States will expire in 2031. The expiration dates above do not include any additional exclusivity available after product approval from patent term extension, supplemental protection certificates and/or pediatric exclusivity.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, import and export of pharmaceutical products, biological products and medical devices, such as those we are developing.

United States drug and biological product approval process

In the United States, the FDA approves new drug products under the Federal Food, Drug, and Cosmetic Act, or FDCA, while new biologic products are licensed for marketing under the Public Health Service Act, or PHSA. Both drugs and biologics are regulated under the FDCA and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval may subject an applicant to a variety of administrative or judicial actions, including, among other things, the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, civil penalties and criminal prosecution.

Generally, the process required by the FDA before a drug or biological product may be marketed in the United States involves the following:

- completion of preclinical laboratory tests and animal studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- completion of process development and manufacturing studies in compliance with current good manufacturing practices, or cGMP, requirements;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
-

performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product and the safety, potency and purity of a candidate biologic product for each indication;

- submission to the FDA of an NDA or an abbreviated new drug application, or ANDA, for a new drug product or BLA for a biological product, as applicable;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- FDA review and approval of the NDA or BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy program and the potential requirement to conduct post-approval studies.

We expect that all of our clinical product candidates will be subject to review as biological products under BLA standards. Although MM-310 contains both drug and biological components, we believe that this combination product would be subject to review as a biological product, pursuant to a BLA.

Preclinical studies and the IND process

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as in vitro and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed protocol for clinical studies, among other things, to the FDA as part of an IND. An IND is an exemption from the FDCA that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and is a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved application. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not necessarily result in the FDA allowing clinical trials to commence.

Clinical trials

Clinical trials involve the administration of the investigational new drug to human subjects – healthy volunteers or patients – under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions. For clinical trials involving an IND, an IRB must operate in compliance with FDA regulations. Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board, or DSMB. This group provides authorization as to whether or not a trial may move forward at designated check points based on access that only the DSMB maintains to available data from the study.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The investigational drug or biological product is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, side effects associated with increasing doses, pharmacological action, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The investigational drug or biological product is administered to a limited patient population to identify common 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. This phase may include

administration of the investigational drug to patients with concomitant disease conditions.

- Phase 3: The investigational drug or biological product is administered to an expanded patient population in adequate and well-controlled clinical trials, typically at geographically dispersed clinical trial sites, to generate sufficient data to statistically confirm the efficacy and safety of the product for approval, to permit the FDA to evaluate the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

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

In some cases, the FDA may approve an application for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to further document a clinical benefit in the case of drugs approved under accelerated approval regulations.

Disclosure of clinical trial information

Sponsors of applicable clinical trials of FDA regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public on the ClinicalTrials.gov website as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Marketing approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's pharmacology chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA or BLA requesting approval to market the product for one or more indications. FDA approval of the NDA or BLA is required before marketing of the product may begin in the United States. Under federal law, the submission of most NDAs and BLAs is subject to a substantial application user fee, currently $2,588,478 for an application requiring clinical data for fiscal year 2019, and the sponsor of an approved NDA or BLA is also subject to annual product or program fees, currently $309,915 per program. These fees may be increased or decreased annually.

The FDA conducts a preliminary review of all NDAs and BLAs within the first 60 days after receipt before accepting them for filing based on the agency's threshold determination that they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the application must be resubmitted with the additional information, which would also be 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 has agreed to specified performance goals in the review of NDAs and BLAs. Most such applications for non-priority products are reviewed within ten to twelve months after filing, and most applications for priority review products, that is, drugs and biologics that the FDA determines represent a significant improvement over existing therapy, are reviewed in six to eight months after filing. The review process may be extended by the FDA for three additional months to consider certain late-submitted information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drugs or biological products or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA or BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

The testing and approval process requires substantial time, effort and financial resources, and each may take many years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to develop our product candidates and secure necessary governmental approvals, which could delay or preclude us from marketing our products.

After the FDA's evaluation of the NDA or BLA and inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug or biological product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

Even if the FDA approves a product, the agency may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions through a Risk Evaluation and Mitigation Strategy or other risk management mechanisms, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, some types of changes to the approved product, such as changes in indications, manufacturing changes and labeling, are subject to further testing requirements and FDA review and approval.

Fast track designation

The FDA is required to facilitate the development and expedite the review of drugs and biologics that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug or biologic candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days after receipt of the sponsor's request.

In addition to other benefits, such as the ability to have more frequent interactions with the FDA, the FDA may initiate review of sections of a fast track product'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 the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA or BLA is submitted. In addition, 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 trial process.

Priority review

Under FDA priority review guidelines, a product candidate may be eligible for review within a six to eight month time frame from the time a complete application is accepted for filing. Products regulated by the FDA's Center for Drug Evaluation and Research, or CDER, are eligible for priority review if they provide a significant improvement compared to marketed products in the treatment, diagnosis or prevention of a disease. Products regulated by the FDA's Center for Biologics Evaluation and Research are eligible for priority review if they provide a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious or life-threatening disease. A fast track designated product candidate would ordinarily meet the FDA's criteria for priority review.

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 provides meaningful therapeutic benefit to patients over existing treatments based on a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. 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 Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Breakthrough therapy designation

The FDA is also required to expedite the development and review of the application for approval of drugs that are intended to treat a serious or life-threatening disease or condition where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. Under the breakthrough therapy program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a breakthrough therapy concurrent with, or after, the filing of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor’s request.

Orphan drugs

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs or biologics intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals 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 or biologic and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation is taken into consideration but generally does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA or BLA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug or biologic for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity in that it is shown to be safer, more effective or makes a major contribution to patient care. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA or BLA application user fee.

Pediatric information and exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA, BLA or supplement to an NDA or BLA must contain data from pediatric studies that are adequate to assess the safety and effectiveness of the drug or biological product 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. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Under the Food and Drug Administration Safety and Innovation Act, or FDASIA, the FDA has additional authority to take action against manufacturers not adhering to pediatric study requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan drug designation.

Pediatric exclusivity is a type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity or patent protection, including the non patent and orphan exclusivity. This six month exclusivity may be granted if an application sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA’s request, the additional protection is granted.

The Hatch-Waxman Act

Abbreviated new drug applications

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent that claims to cover the applicant’s product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA’s Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an ANDA. Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants

are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as “generic equivalents” to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA’s Orange Book. Specifically, the applicant must certify that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid is called a Paragraph IV certification. If the ANDA applicant does not challenge the listed patents, the ANDA will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of a 30 month period, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that the patent involved is deemed invalid or not infringed.

The ANDA also will not be approved until any applicable 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. Federal law provides a period of five years following approval of a drug containing no previously approved active ingredients during which ANDAs for generic versions of those drugs cannot be received by the FDA, except that the application may be submitted in four years if it contains a Paragraph IV certification. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and thus, no ANDA may be filed before the expiration of the exclusivity period. Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor, during which the FDA cannot grant effective approval of an ANDA based on that listed drug.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA's drug shortage list. The FDA must also expedite review of ''competitor generic therapies'' or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

Patent term extension

After NDA approval, owners of relevant drug patents may apply for up to a five year patent term extension. The allowable patent term extension is calculated as half of the drug's testing phase, based on the time between IND application and submission of the NDA, and all of the review phase, based on the time between the NDA submission and approval up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years.

For patents that might expire during the application phase, the patent owner may request an interim patent term extension. An interim patent term extension increases the patent term by one year and may be renewed up to four times. For each interim patent term extension granted, the post-approval patent term extension is reduced by one year. The director of the U.S. Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent term extension is being sought is likely. Interim patent term extensions are not available for a drug for which an NDA has not been submitted.

Section 505(b)(2) new drug applications

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A 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 previous approval of a similar 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. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new 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 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.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a Section 505(b)(2) NDA 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 a 30 month period, settlement of the lawsuit or a decision in the infringement case that the patent involved is deemed invalid or not infringed.

Combination products

A combination product is a product comprised of (i) two or more regulated components (i.e., drug/device, biologic/device, drug/biologic or drug/device/biologic) that are physically, chemically, or otherwise combined or mixed and produced as a single entity; (ii) two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products; (iii) a drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where, upon approval of the proposed product, the labeling of the approved product would need to be changed (e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose); or (iv) any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

The FDA is divided into various branches, or Centers, by product type. Different Centers typically review drug, biologic or device applications. In order to review an application for a combination product, the FDA must decide which Center should be responsible for the review. FDA regulations require that the FDA determine the combination product's primary mode of action, or PMOA, which is the single mode of a combination product that provides the most important therapeutic action of the combination product. The Center that regulates that portion of the product that generates the PMOA or that has expertise in the relevant therapeutic area becomes the lead evaluator. If there are two independent modes of action, neither of which is subordinate to the other, the FDA makes a determination as to which Center to assign the product based on consistency with other combination products raising similar types of safety and effectiveness questions or to the Center with the most expertise in evaluating the most significant safety and effectiveness questions raised by the combination product. When evaluating an application, a lead Center may consult other Centers but still retain complete reviewing authority, or it may collaborate with another Center, by which the lead Center assigns review of a specific section of the application to another Center, delegating its review authority for that section. Typically, the FDA requires a single marketing application submitted to the Center selected to be the lead evaluator, although the agency has the discretion to require separate applications to more than one Center. One reason to submit multiple evaluations is if the applicant wishes to receive some benefit that accrues only from approval under a particular type of application, like new drug product exclusivity. If multiple applications are submitted, each application may be evaluated by a different lead Center.

Biosimilars law

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, amended the PHSA to create a new licensure framework for biosimilar products, which could ultimately subject our biological products to competition. Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a referenced, branded biologic product. Previously, there had been no licensure pathway for such biosimilar or interchangeable products. For purposes of the BPCIA, a reference product is defined as the single

biological product licensed under a full BLA against which a biological product is evaluated in an application submitted under a follow-on BLA. Biosimilarity sufficient to reference a prior FDA-approved product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity must be shown through analytical studies, animal studies, and at least one clinical trial, absent a waiver by the Secretary of the U.S. Department of Health & Human Services. A biosimilar product may be deemed interchangeable with a prior approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

The BPCIA also created a 12-year period of reference product exclusivity, which can be extended to 12½ years with pediatric exclusivity. The 12-year exclusivity period begins on the date of first licensure of the reference product under the PHSA and during which the licensure of a follow-on application for a biosimilar or interchangeable product cannot be made effective. During the first four years (or four and one-half years with pediatric exclusivity) of the 12-year period, an application for a biosimilar or interchangeable version of the reference product cannot be submitted to the FDA.

The BPCIA includes limits on obtaining 12-year reference product exclusivity for certain changes or modifications to the reference product. A separate 12-year reference product exclusivity period does not apply to:

- a BLA supplement for the product that is the reference product;
- a subsequent BLA filed by the same reference product sponsor or manufacturer (or a licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength; or
- a modification to the structure of the biological product that does not result in a change in safety, purity or potency.

The FDA has not yet issued proposed regulations setting forth its interpretation of the BPCIA's provisions but has issued guidance documents and draft guidance documents related to BPCIA implementation concerning biosimilarity and interchangeability, BLA submission requirements, exclusivity, clinical pharmacology, statistics, labeling and naming. As of February 1, 2019, the FDA has approved 17 biosimilar products for use in the United States. No interchangeable biosimilars have been approved.

In addition to creating a 12-year period of reference product exclusivity, the BPCIA clarifies the interaction of that exclusivity with orphan drug exclusivity, such that the licensure of a biosimilar or interchangeable version of a reference product that was designated and approved as an orphan drug may only occur after the later of the expiration of any applicable seven-year orphan drug exclusivity or the 12-year reference product exclusivity (or seven and one-half years and 12½ years with pediatric exclusivity).

Like pediatric exclusivity applicable to drug products approved under the FDCA, pediatric exclusivity applicable to biological reference products is subject to an exception. Pediatric exclusivity will not apply to either the 12-year reference product or the seven-year orphan drug exclusivity periods if the FDA determines later than nine months prior to the expiration of such period that the study reports a BLA sponsor submitted in response to a written request for pediatric studies met the terms of that request.

Our investigational biological products, if approved, could be considered reference products entitled to 12-year exclusivity. Even if our products are considered to be reference products eligible for exclusivity, another company could market a competing version of any of our biological products if the FDA approves a full BLA for such 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 sets forth a complex mechanism for resolving patent disputes that involves a step-wise exchange of information prior to the initiation of a patent infringement lawsuit against a biosimilar or interchangeable product sponsor. Unlike the Hatch-Waxman Act, the BPCIA provides no automatic stay on approval of a biosimilar or interchangeable product application.

Overview of FDA regulation of companion diagnostics

We are developing in vitro diagnostics for use in selecting the patients that we believe will respond to our cancer therapeutics.

The FDA published final guidance in July 2014 that addresses issues critical to developing in vitro companion diagnostics. The guidance provides that in vitro companion diagnostics that are essential for the safe and effective use of a corresponding therapeutic product must be approved contemporaneously with that therapeutic in most circumstances. Based on the guidance and the FDA's past treatment of companion diagnostics, we believe that the FDA will likely require one or more of our in vitro diagnostics to obtain premarket approval, or PMA, in conjunction with approval of the associated therapeutic, which will involve coordination of review by CDER and by the FDA's

Center for Devices and Radiological Health Office of In Vitro Diagnostics and Radiological Health.

Diagnostic tests determined by the FDA to be useful, but not essential, for the safe and effective use of a corresponding therapeutic product are also subject to the same medical device pathways, but their clearance or approval would not be subject to a coordinated review of the diagnostic test and the therapeutic product.

The FDA classifies medical devices into one of three classes. Devices deemed to pose lower risk are placed in either Class I or II, which requires the manufacturer to submit to the FDA a premarket notification requesting permission for commercial distribution. Some low risk devices are exempt from this requirement. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life-supporting or implantable devices, or devices deemed not substantially equivalent to a previously cleared 510(k) device, are placed in Class III, requiring a PMA. A medical device, including an in vitro diagnostic, or IVD, to be commercially distributed in the United States must receive either 510(k) clearance or PMA (or be a Class I exempt device that does not require pre-market review) from the FDA prior to marketing. The FDA has previously required in vitro companion diagnostics intended to select the patients who will respond to the product candidate to obtain a PMA simultaneously with approval of the product candidate.

510(k) clearance pathway

If any of the diagnostic products under development were determined by FDA not to be essential to the safe and effective prescription of a corresponding therapeutic product, it is possible that the diagnostic test could require 510(k) clearance. The FDA's 510(k) clearance pathway usually takes from three to twelve months, but it can take significantly longer. The FDA may require additional information, including clinical data, to make a determination regarding substantial equivalence.

After a device receives 510(k) clearance, any modification that could significantly affect its safety or effectiveness, or that would constitute a new or major change in its intended use, would require a new 510(k) clearance or, depending on the modification, a PMA. The FDA requires each manufacturer to determine whether the proposed change requires submission of a 510(k) notice or a PMA, but the FDA can review any such decision and can disagree with a manufacturer's determination. If the FDA disagrees with a manufacturer's determination, the FDA can require the manufacturer to cease marketing and/or recall the modified device until 510(k) clearance or a PMA is obtained. If the FDA requires us to seek 510(k) clearance or a PMA for any modifications to a previously cleared product, we may be required to cease marketing or recall the modified device until we obtain this clearance or approval. Also, in these circumstances, we may be subject to significant regulatory fines or penalties.

PMA pathway

Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life supporting or implantable devices, or devices deemed not substantially equivalent to a previously 510(k) cleared device or a preamendment Class III device for which PMA applications have not been called, are placed in Class III, requiring PMA. The PMA pathway requires proof of the safety and effectiveness of the device to the FDA's satisfaction. The PMA pathway generally takes from one to three years or longer from submission of the application. Most companion diagnostic tests have been classified as Class III devices subject to the PMA pathway.

A PMA application for an IVD must provide extensive preclinical and clinical trial data. Preclinical data for an IVD includes many different tests, including how reproducible the results are when the same sample is tested multiple times by multiple users at multiple laboratories. The clinical data need to establish that the test is sufficiently safe, effective and reliable in the intended use population. In addition, the FDA must be convinced that a device has clinical utility, meaning that an IVD provides information that is clinically meaningful. A biomarker's clinical significance may be obvious, or the applicant may be able to rely upon published literature or submit data to show clinical utility.

A PMA application also must provide information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee; for fiscal year 2019, the standard fee for review of a PMA is $322,147 and the small business fee for review of a PMA is $80,537.

As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with Quality System Regulation, or QSR, requirements, which impose elaborate design control, testing, manufacturing, control, documentation and other quality assurance procedures.

Upon submission, the FDA determines if the PMA application is sufficiently complete to permit a substantive review, and, if so, the FDA accepts the application for filing. The FDA then commences an in-depth review of the PMA application. The entire process typically takes one to three years, but may take longer. The review time is often significantly extended as a result of the FDA asking for more information or clarification of information already provided. The FDA also may respond with a not approvable determination based on deficiencies in the application and require additional clinical trials that are often expensive and time-consuming and can substantially delay approval. During the review period, an FDA advisory committee, typically a panel of clinicians, likely will be convened to

review the application and recommend to the FDA whether, or upon what conditions, the device should be approved. Although the FDA is not bound by the advisory panel decision, the panel's recommendation is important to the FDA's overall decision making process.

If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the manufacturer. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Failure to comply with the conditions of approval can result in material adverse enforcement action, including the loss or withdrawal of the approval.

Even after approval of a PMA, a new PMA or PMA supplement may be required in the event of a modification to the device, its labeling or its manufacturing process. Supplements to a PMA often require the submission of the same type of information required for an original PMA, except that the supplement is generally limited to the information needed to support the proposed change from the product covered by the original PMA.

Clinical trials

A clinical trial is almost always required to support a PMA application. All clinical trials of investigational devices must be conducted in compliance with the FDA's requirements. If an investigational device could pose a significant risk to patients pursuant to FDA regulations, the FDA must approve an Investigational Device Exemption, or IDE, application prior to initiation of investigational use. IVD trials usually do not require an IDE, as the FDA does not judge them to be a significant risk, either because the results do not affect the patients in the study or because obtaining a sample from the patient is not by means of a high risk or invasive procedure. However, for a trial where the IVD result directs the therapeutic care of patients with cancer (companion diagnostics) or the IVD sampling is invasive, we believe that the FDA would consider the investigation to present significant risk and require an IDE.

An IDE application must be supported by appropriate data, such as laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The FDA typically grants IDE approval for a specified number of patients. A nonsignificant risk device does not require FDA approval of an IDE. Both significant risk and nonsignificant risk investigational devices require approval from IRBs at the study centers where the device will be used.

During the trial, the sponsor must comply with the FDA's IDE requirements for investigator selection, trial monitoring, reporting and record keeping. The investigators must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of investigational devices and comply with all reporting and record keeping requirements. Prior to granting PMA, the FDA typically inspects the records relating to the conduct of the study and the clinical data supporting the PMA application for compliance with applicable requirements.

Although the QSR does not fully apply to investigational devices, the requirement for controls on design and development does apply. The sponsor also must manufacture the investigational device in conformity with the quality controls described in the IDE application and any conditions of IDE approval that the FDA may impose with respect to manufacturing.

Post-market

After a device is on the market, numerous regulatory requirements apply. These requirements include: the QSR, labeling regulations, the FDA's general prohibition against promoting products for unapproved or "off label" uses, the Medical Device Reporting regulation, which requires that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if it were to recur, and the Reports of Corrections and Removals regulation, which requires manufacturers to report recalls and field actions to the FDA if initiated to reduce a risk to health posed by the device or to remedy a violation of the FDCA.

The FDA enforces these requirements by inspection and market surveillance. If the FDA finds a violation, it can institute a wide variety of enforcement actions, ranging from a public warning letter to more severe sanctions such as: fines, injunctions and civil penalties; recall or seizure of products; operating restrictions, partial suspension or total shutdown of production; refusing requests for PMA of new products; withdrawing PMAs already granted; and criminal prosecution.

Other regulatory requirements

Any drug or biological products manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse drug experiences. 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.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. 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. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug or biologic.

In addition, drug and biologic manufacturers and other entities involved in the manufacture and distribution of approved drugs and biological products are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. The FDA was also granted new inspection authorities under FDASIA. 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 us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards 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, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical trials to assess new safety risks or imposition of distribution or other restrictions under a Risk Evaluation and Mitigation Strategy 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;
- fines, untitled and warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
    - product seizure or detention, or refusal to permit the import or export of products; or
- consent decrees, injunctions or the imposition of civil or criminal prosecution.

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. If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products.

Additional provisions

Anti-kickback and false claims laws

In addition to FDA restrictions on marketing of pharmaceutical products, pharmaceutical companies that participate in federal healthcare programs like Medicare or Medicaid are subject to various U.S. federal and state laws that may restrict certain marketing practices. These laws include but are not limited to anti-kickback statutes and false claims statutes. The federal anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. The Patient Protection and Affordable Care Act as amended by the Health Care Education and Reconciliation Act of 2010, collectively the Health Care Reform Laws, amended the intent element of the anti-kickback statute such that liability under the statute can be proved even if a person or entity does not have

actual knowledge of the statute or specific intent to violate it. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. In addition to the federal anti-kickback statute, the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, makes it a crime to knowingly and willfully execute or attempt to execute a scheme to defraud any healthcare benefit program

The federal civil False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Government enforcement agencies and private whistleblowers have initiated investigations or brought private lawsuits against pharmaceutical companies for a variety of allegedly improper promotional or marketing activities, such as allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product, or for engaging in promotion for "off-label" uses. Additionally, the Health Care Reform Laws amended the federal False Claims Act such that a violation of the federal anti-kickback statute can serve as a basis for liability under the False Claims Act. In addition to the federal civil False Claims Act, the federal false statements statute prohibits, among other things, knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

The majority of states also have statutes or regulations similar to the federal anti-kickback statute and/or False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. In addition, the federal transparency law under the Health Care Reform Laws, known as the Open Payments program, requires manufacturers of drugs, devices, biologics and medical supplies reimbursable under Medicare or Medicaid to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals, as well as physician ownership and investment interests, and provides for public reporting of the data reported by manufacturers.

Government price reporting

We would be required to report certain price data and pay certain rebates to the U.S. government as a condition of participation in federal healthcare programs. Medicaid is jointly administered by federal and state governments for the benefit of low income and certain disabled beneficiaries. Under the Medicaid Drug Rebate Program, we would be required to pay a certain rebate for each unit of product reimbursed by the state Medicaid programs.

Data protection

We are subject to data protection laws and regulations (i.e., laws and regulations that address privacy and data security). The legislative and regulatory landscape for data protection continues to evolve, and in recent years there has been an increasing focus on privacy and data security issues. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws and federal and state consumer protection laws govern the collection, use, disclosure and protection of health-related and other personal information. Failure to comply with data protection laws and regulations could result in government enforcement actions (which could include civil or criminal penalties), private litigation and/or adverse publicity and could negatively affect our operating results and business. In addition, we may obtain health information from third parties (e.g., healthcare providers who prescribe our products) that are subject to privacy and security requirements under HIPAA. We could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information in a manner that is not authorized or permitted.

Foreign regulation

In order to market any therapeutic or diagnostic product outside of the United States, we need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we need to 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 from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

The European Medicines Agency, or EMA, grants orphan medicinal product designation to promote the development of products that may offer therapeutic benefits for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the European Union. In addition, orphan medicinal product designation can be granted if the drug is intended for a life threatening, seriously debilitating or serious and chronic condition and without incentives it is unlikely that sales of the drug in the European Union would be sufficient to justify developing the drug. Orphan medicinal product designation is only available if there is no other satisfactory method approved in the European Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan medicinal product will be of significant benefit to patients. Orphan medicinal product designation provides opportunities for free protocol assistance and fee reductions for access to the centralized regulatory procedures. Orphan medicinal product designation also provides ten years of market exclusivity following drug approval. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Clinical trial approval

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on GCP, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No. 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. The new Clinical Trials Regulation will become directly applicable to and binding in all European Union Member States without the need for any national implementing legislation. The new Clinical Trials Regulation (EU) No. 536/2014 will become applicable in or after 2019. It will overhaul the current system of approvals for clinical trials in the European Union and is aimed specifically at simplifying and streamlining the approval of clinical trials in the European Union.

Conditional marketing authorization

In the European Union, the EMA supports the development of medicines that address unmet medical needs of patients. In the interest of public health, applicants may be granted a conditional marketing authorization for such medicines where the benefit of immediate availability outweighs the risk of less comprehensive data than normally required, based on the scope and criteria defined in legislation and guidelines.

Medicines for human use are eligible if they belong to at least one of these categories:

- aimed at treating, preventing or diagnosing seriously debilitating or life-threatening diseases;
- intended for use in emergency situations (also less comprehensive pharmaceutical and non-clinical data may be accepted for such products);
- designated as orphan medicines.

Conditional marketing authorization may be granted if the CHMP finds that all the following requirements are met:

- the benefit-risk balance of the product is positive;
- it is likely that the applicant will be able to provide comprehensive data;
- unmet medical needs will be fulfilled;
- the benefit to public health of the medicinal product's immediate availability on the market outweighs the risks due to need for further data.

Brexit and the regulatory framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as Brexit). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provided notice of withdrawal. Since the regulatory framework for pharmaceutical products in the United Kingdom is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product

candidates and products in the United Kingdom.

Foreign Corrupt Practices Act

Various federal and foreign laws govern our international business practices with respect to payments to government officials. Those laws include the U.S. Foreign Corrupt Practices Act, or FCPA, which prohibits U.S. companies and their representatives from paying, offering to pay, promising or authorizing the payment of anything of value to any foreign government official, government staff member, political party or political candidate for the purpose of obtaining or retaining business or to otherwise obtain favorable treatment or influence a person working in an official capacity. In many countries, the healthcare professionals we may interact with may meet the FCPA's definition of a foreign government official. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect their transactions and to devise and maintain an adequate system of internal accounting controls.

We are subject also to the U.K. Bribery Act 2010, or Bribery Act, which proscribes giving and receiving bribes in the public and private sectors, bribing a foreign public official, and failing to have adequate procedures to prevent employees and other agents from giving bribes. U.S. companies that conduct business in the United Kingdom generally will be subject to the Bribery Act. Penalties under the Bribery Act include potentially unlimited fines for companies and criminal sanctions for corporate officers under certain circumstances. Other countries have enacted similar anti-corruption laws and/or regulations.

21st Century Cures Act and new FDA regulations

In December 2016, Congress passed the 21st Century Cures Act, or the Cures Act. This law is intended to enable the acceleration of the discovery, development and delivery of 21st century cures, among other things. Provisions in that law, such as those applying to precision medicine, technical updates to clinical trial databases and advancing new drug therapies, could apply directly or indirectly to our activities. At this point, however, it is not clear how that law will be implemented and what effect it may have on our business.

In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations changed or what the effect of such changes, if any, may be.

Healthcare reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. By way of example, the U.S. and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the U.S. Congress enacted the Affordable Care Act, or ACA, which, among other things, includes changes to the coverage and payment for products under government healthcare programs.

Since enactment of the ACA, there have been numerous legal challenges and legislative actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, the U.S. Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the U.S. 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, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the U.S. Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing.

Pharmaceutical coverage, pricing and reimbursement

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown

significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for any drug products for which we obtain regulatory approval and could adversely affect our net revenue and results.

Beyond the United States, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any of our products.

Employees

As of February 28, 2019, we had 27 full-time employees, of whom 16 are engaged in research and development. None of our employees is represented by a labor union or covered by collective bargaining agreements.

On November 7, 2018, we announced that we were implementing a reduction in headcount as part of a corporate restructuring, after which we expected to have approximately 27 employees. The corporate restructuring followed a comprehensive review of our drug candidate pipeline. The reduction in headcount was completed in February 2019.

We consider our relationship with our employees to be good.

Financial Information

Financial information is provided in our consolidated financial statements included in this Annual Report on Form 10-K and in Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Information about our dependence on limited amounts of customers is provided in Note 1, "Nature of the Business and Summary of Significant Accounting Policies – Concentration of Credit Risk" in the accompanying notes to the consolidated financial statements.

In August 2010, we acquired a controlling financial interest in Silver Creek Pharmaceuticals Inc., or Silver Creek. At such time we had the ability to direct the activities of Silver Creek that most significantly impacted Silver Creek's economic performance through our ownership percentage and through the board of director seats we controlled, and as such Silver Creek was consolidated in our financial statements. In the third quarter of 2017, Silver Creek completed its Series C preferred stock financing, which reduced our ownership percentage of Silver Creek below 50% and resulted in us no longer controlling the Silver Creek board of directors, and as a result Silver Creek was deconsolidated from our financial statements. Information about the deconsolidation of Silver Creek from our financial statements is provided in Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

Our Corporate Information

We were originally incorporated in the Commonwealth of Massachusetts in 1993 and reincorporated under the laws of the State of Delaware in October 2010. Our principal executive offices are located at One Kendall Square, Suite B7201, Cambridge, MA 02139, and our telephone number is (617) 441-1000.

Information Available on the Internet

We maintain a website with the address www.merrimack.com. We are not including the information contained on our website as a part of, or incorporating it by reference into, this Annual Report on Form 10-K. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through the "SEC Filings" link in the "Investors" section of our website as soon as reasonably practicable after those materials have been electronically filed with, or furnished to, the Securities and Exchange Commission, or the SEC. We also make available on our website our corporate governance guidelines, the charters for our audit committee, corporate governance and nominating committee, and organization and compensation committee, and our code of business conduct and ethics, which applies to our directors, officers and employees, and such information is available in print and free of charge to any of our stockholders who requests it. In addition, we intend to disclose on our website any amendments to, or waivers from, our code of business conduct and ethics that are required to be publicly disclosed pursuant to rules of the SEC.

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Item 1A. Risk Factors

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 2 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to the Sale of the Commercial Business to Ipsen

Because the commercial business represented all of our revenues for fiscal year 2016 and the three months ended March 31, 2017, our business following the sale of the commercial business is substantially different than it was prior to such sale.

As a result of the completion of the asset sale with Ipsen, Ipsen acquired our right, title and interest in the commercial business. The commercial business represented all of our revenues for the fiscal year 2016 and the three months ended March 31, 2017. Following the asset sale, we retained only the pipeline business. Our results of operations and financial condition may be materially affected if we fail to grow the remaining pipeline business, if we are unable to raise additional capital when needed to run the remaining pipeline business, if we must incur significant costs in order to raise additional capital to run the remaining pipeline business or if we are unable to successfully develop and commercialize our remaining product candidates.

We have been, and in the future may be, subject to securities litigation, which is expensive and could divert our attention.

We have been, and may in the future be, subject to securities class action litigation. Securities litigation against us could result in substantial costs and divert our management's attention, which could seriously harm our business. For instance, a putative stockholder class action suit was filed by a purported stockholder of ours in the Superior Court of Massachusetts for the County of Middlesex against us and our directors. The case was captioned Robert Garfield v. Merrimack Pharmaceuticals Inc., et al., or the Garfield Action. The Garfield Action complaint alleged that our directors breached their fiduciary duties by entering into the asset sale agreement and that the definitive proxy statement relating to the asset sale contained inadequate disclosures and omissions. Although we believed that the Garfield Action was without merit, to avoid the risk of the litigation delaying or adversely affecting the asset sale and to minimize the expense of defending the litigation related to the asset sale, we agreed to make supplemental disclosures related to the asset sale and to pay the plaintiff's counsel $375,000 in attorney's fees in connection with the resolution of the Garfield Action. As a result, the plaintiff concluded that the claims in the Garfield Action were mooted, and the Garfield Action was dismissed with prejudice. Nonetheless, there can be no guarantee that there will not be additional securities class action litigation in connection with the asset sale.

There can be no guarantee that Ipsen will comply with its obligation to use commercially reasonable efforts in connection with the development of ONIVYDE or that the milestones set forth in the Servier agreement will be achieved.

Ipsen has agreed to use commercially reasonable efforts to develop ONIVYDE in connection with obtaining the regulatory approval by the FDA of ONIVYDE for certain indications. Although the results of this approval process may enable Ipsen to achieve the milestones necessary for us to receive the contingent payments under the asset sale agreement, there is no guarantee that Ipsen will take the steps set forth in the asset sale agreement and that such development will lead to the successful approval of ONIVYDE for such additional indications. Therefore, there can be

no guarantees that any of the milestones set forth in the asset sale agreement will be achieved and that we will receive any future contingent payments.

Additionally, although the asset sale agreement entitles us to receive certain net milestone payments of up to $33.0 million that may become payable under the Servier agreement, to date we have received only $28.0 million of such net milestone payments. Payment of the remaining $5.0 million is not guaranteed for the milestone related to the first patient dosed in a pivotal clinical trial of ONIVYDE in an indication other than pancreatic cancer, as the satisfaction of such milestone is based on a clinical trial being conducted by Ipsen and Servier and is therefore out of our control.

Ipsen did not assume any of the excluded liabilities under the asset sale agreement.

Pursuant to the asset sale agreement, Ipsen assumed only certain specified liabilities set forth in the asset sale agreement and did not assume all of the liabilities associated with the commercial business. Certain liabilities remain with us post-closing. While we believe that we have adequately accrued for these liabilities or are adequately insured against certain of the risks associated with such excluded liabilities, there can be no assurances that additional expenditures will not be incurred in resolving any such liabilities.

The asset sale agreement may expose us to contingent liabilities.

We have agreed to indemnify Ipsen for certain breaches of representations, warranties or covenants made by us in the asset sale agreement and for certain specified existing litigation. We have agreed that if we cannot pay our indemnification obligations, Ipsen will have set-off rights against any future contingent payments. Significant indemnification claims by Ipsen could further materially and adversely affect our financial condition and/or significantly reduce any future contingent payments.

Risks Related to Our Financial Position and Need for Additional Capital

We are engaged in a strategic review process that could significantly impact our future operations and financial position. However, we cannot provide any commitment regarding when or if this process will result in any type of transaction or any other specific action.

On November 7, 2018, we announced that we have initiated a process to evaluate a full range of strategic alternatives to maximize stockholder value and have retained external advisors to assist in this effort. Although this process could result in potential changes to our current business strategy and future operations, we cannot be sure when or if this process will result in any type of transaction or any other specific action by us. Even if we pursue a transaction, such transaction may not be consistent with our stockholders' expectations or may not ultimately be favorable for our stockholders, either in the shorter or longer term. The review process will require additional resources and costs and may contribute to increased uncertainty, each of which may adversely impact our business and financial position.

We have incurred significant losses since our inception. We expect to incur operating losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss from continuing operations before income tax benefit was $68.5 million for the year ended December 31, 2018 and $118.4 million for the year ended December 31, 2017. As of December 31, 2018, we had an accumulated deficit of $523.3 million. To date, we have financed our operations primarily through private placements of convertible preferred stock, collaborations, public offerings of our securities, secured debt financings, sales of ONIVYDE and the asset sale. We have devoted substantially all of our efforts to research and development, including clinical trials and recently to commercialization of our first product, ONIVYDE, which was sold to Ipsen. We have not completed development of or commercialized any other product candidates or diagnostics other than ONIVYDE. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our expenses would increase substantially to the extent that we:

- continue clinical trials of our product candidates;
- continue the research and development of our other product candidates;
- seek to discover additional product candidates; and
- continue to provide the operational, financial and management information systems and personnel to support our product development.

To become and remain profitable, we must succeed in developing and commercializing products 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 of our product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling or partnering those products for which we may seek and receive regulatory approval. We may never succeed in these activities and may never generate revenues that are significant or large enough 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. Our 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 our stockholders to lose all or part of their investment.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We will need substantial additional funding in connection with our continuing operations. We expect to continue to incur significant research and development expenses in connection with our ongoing activities, particularly as we continue the research, development and clinical trials of, and seek regulatory approval for, our product candidates. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or commercialization efforts.

We believe that our financial resources as of December 31, 2018 and as a result of the corporate restructuring announced on November 7, 2018, together with other restructuring and cost cutting measures that we could implement in the future, provide us with the potential to fund our operations, including debt service obligations and capital expenditure requirements, into at least the second half of 2022. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, and the extent to which we may utilize collaborations with third parties to participate in their development and commercialization, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials. Our future capital requirements will depend on many factors, including:

- the progress and results of the clinical trials of our product candidates;
- our ability to establish and maintain additional collaborations on favorable terms, and the success of any such future collaborations;
- the timing and amount of potential milestone payments related to ONIVYDE that we may receive from Ipsen and Servier;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our product candidates;
- the costs, timing and outcome of regulatory review of our current and future product candidates;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; and
- the extent to which we acquire or invest in businesses, products and technologies.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data required to obtain regulatory approval and, even if regulatory approval is obtained, achieve product sales of any of our product candidates. In addition, any of our product candidates, even if approved, may not achieve commercial success. If we fail to generate sufficient revenues from collaborations or the commercialization of any of our product candidates, we will need to continue to rely on additional financing to achieve our business objectives.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

We do not have any committed external source of funds. Sources of funds may not be available or, if available, may not be available on terms satisfactory to us and could result in significant stockholder dilution.

Until such time, if ever, as we can generate sufficient product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, licensing arrangements and other marketing and distribution arrangements. We also could engage in discussions with third parties regarding partnerships, joint ventures, combinations or divestitures of one or more of our product candidates as we seek to further the development of our research programs, improve our cash position and maximize stockholder value. There can be no assurance as to the timing, terms or consummation of any financing, collaboration, licensing arrangement or other marketing and distribution arrangement, partnership, joint venture, combination or divestiture.

On December 15, 2017, we filed a registration statement on Form S-3 with the SEC to allow the issuance of our securities from time to time in one or more offerings of up to $150,000,000 in aggregate dollar amount. This registration statement was declared effective by the SEC on January 5, 2018. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include

covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, and these covenants may also require us to attain certain levels of financial performance and we may not be able to do so; any such failure may result in the acceleration of such debt and the foreclosure by our creditors on the collateral we used to secure the debt. The debt issued in a debt financing would also be senior to our outstanding shares of capital stock upon our liquidation. Significant indebtedness and the pledge of our assets as collateral in the future could limit our ability to obtain additional debt financing. If we raise additional funds through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. 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.

Our substantial indebtedness may limit cash flow available to invest in the ongoing needs of our business.

On July 2, 2018, we entered into the Loan and Security Agreement, or Loan Agreement, with Hercules Capital, Inc., or Hercules. The Loan Agreement provided for a term loan advance of $15.0 million, which closed on July 2, 2018. The Loan Agreement contains certain events of default, including nonpayment, breach of covenants, representations and warranties, material adverse effect (not including clinical trial failures), insolvency and bankruptcy, judgments, cross default to other indebtedness, and suspension of trading.

In addition to the debt under the Loan Agreement, we have had in the past, and may in the future have, a significant amount of indebtedness. In July 2013, we issued $125.0 million aggregate principal amount of 4.50% convertible notes due 2020, or convertible notes. In December 2015, we issued $175.0 million aggregate principal amount of 11.50% senior secured notes due 2022, or 2022 notes. Although we used a portion of the proceeds from the asset sale to fully extinguish the 2022 notes, and we have extinguished all but $56,000 of the aggregate remaining principal amount of the convertible notes, we could in the future incur additional indebtedness.

Substantial debt combined with our other financial obligations and contractual commitments could have significant adverse consequences, including:

- requiring us to dedicate a substantial portion of cash flow from operations to the payment of interest on, and principal of, our debt, which will reduce the amounts available to fund working capital, capital expenditures, product development efforts and other general corporate purposes;
- increasing our vulnerability to adverse changes in general economic, industry and market conditions;
- obligating us to restrictive covenants that may reduce our ability to take certain corporate actions or obtain further debt or equity financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we compete; and
- placing us at a competitive disadvantage compared to our competitors that have less debt or better debt servicing options.

In addition, we are vulnerable to increases in the market rate of interest because our currently outstanding secured debt bears interest at a variable rate. If the market rate of interest increases, we will have to pay additional interest on our outstanding debt, which would reduce cash available for our other business needs.

We intend to satisfy our current and future debt service obligations with our existing cash and cash equivalents and funds from external sources, if any. However, we may not have sufficient funds or may be unable to arrange for additional financing to pay the amounts due under our existing debt. To the extent we seek funds from external sources in the future, such funds may not be available on acceptable terms, if at all. In addition, a failure to comply with the covenants under our existing debt instrument or any future debt instruments could result in an event of default under those instruments. In the event of an acceleration of amounts due under our debt instruments as a result of an event of default, including upon the occurrence of an event that would reasonably be expected to have a material adverse effect on our business, operations, properties, assets or condition or a failure to pay any amount due, we may not have sufficient funds or may be unable to arrange for additional financing to repay our indebtedness or to make any accelerated payments, and the lenders could seek to enforce security interests in the collateral securing such indebtedness. In addition, the covenants under our existing debt instrument and the pledge of our assets as collateral limit our ability to obtain additional debt financing.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains

significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

We might not be able to utilize our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2018, we had federal net operating loss carryforwards of $179.7 million, which begin to expire in 2034, and state net operating loss carryforwards of $263.9 million, which begin to expire in 2031. As of December 31, 2018, we also had federal research and development tax credit carryforwards of $28.8 million and state research and development tax credit carryforwards $18.9 million, which begin to expire in 2022 and 2025, respectively. These net operating loss and tax credit carryforwards could expire unused or could be unavailable to offset our future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain how various states will respond to the newly enacted federal tax law. If our ability to use our historical net operating loss and tax credit carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

Our investments are subject to risks that could result in losses.

We have invested and plan to continue to invest our cash in a variety of financial instruments, principally securities issued by the U.S. government and its agencies, investment grade corporate bonds, including commercial paper, and money market instruments. All of these investments are subject to credit, liquidity, market and interest rate risk. Such risks, including the failure or severe financial distress of the financial institutions that hold our cash, cash equivalents and investments, may result in a loss of liquidity, impairment to our investments, realization of substantial future losses, or a complete loss of the investments in the long-term, which may have a material adverse effect on our business, results of operations, liquidity and financial condition. In order to manage the risk to our investments, we maintain an investment policy that, among other things, limits the amount that we may invest in any one issue or any single issuer and requires us to only invest in high credit quality securities, but there can be no guarantee that our investments will not result in losses.

A decrease in the carrying value of our equity holdings in Silver Creek could adversely affect our balance sheet.

In August 2010, we acquired 12,000,000 shares of Series A preferred stock of Silver Creek in exchange for our grant to Silver Creek of technology licenses. As these shares represented a controlling financial interest, we consolidated Silver Creek in our consolidated financial statements. In the third quarter of 2017, Silver Creek completed its Series C preferred stock financing, which reduced our ownership percentage of Silver Creek below 50% and resulted in us deconsolidating Silver Creek from our consolidated financial statements. As a result of the deconsolidation, we now account for our investment in Silver Creek under the equity method of accounting. The carrying value of our shares of Series A preferred stock of Silver Creek was $7.4 million at December 31, 2018. There can be no guarantee that the value of our investment in Silver Creek will not realize a substantial future loss or complete loss of value, which would in turn adversely affect our balance sheet. On a quarterly basis, we review the investment for impairment whenever events or changes in circumstances indicate that the carrying amount of the investment might not be recoverable. These circumstances can include, but are not limited to, negative current events or long-term outlooks impacting Silver Creek and/or its programs, planned or announced delays in the clinical development process to advance its programs, a current fair value of investment at a lower value than our investment and/or investors no longer providing financial support or reducing their financial commitment to Silver Creek.

Risks Related to the Development and Commercialization of Our Product Candidates

We depend heavily on the success of our product candidates. All of our product candidates are in preclinical and clinical development. Clinical trials of our product candidates may not be successful. If we are unable to successfully commercialize our product candidates, or experience significant delays in doing so, our business will be materially

harmed.

We invest a significant portion of our efforts and financial resources in the development of our product candidates for the treatment of various types of cancer. All of our product candidates are still in preclinical and clinical development. Our ability to generate meaningful product revenues will depend heavily on the successful development of our product candidates. The success of our product candidates, which include both our product candidates and companion diagnostic candidates, will depend on several factors, including the following:

- successful enrollment in, and completion of, preclinical studies and clinical trials;
- receipt of marketing approvals from the FDA and similar regulatory authorities outside the United States for our product candidates, including our diagnostics;
- establishing commercial manufacturing capabilities, which we anticipate doing primarily through arrangements with third-party manufacturers;
- launching commercial sales of any approved products, whether alone or in collaboration with others;

- acceptance of any approved products by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- a continued acceptable safety profile of any products following approval; and
- qualifying for, maintaining, enforcing and defending intellectual property rights and claims.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully develop our product candidates, which would materially harm our business.

For example, in November 2018, we announced that we are discontinuing development of all ongoing MM-121 programs based on the results of the interim analysis of the SHERLOC clinical trial that were announced on October 19, 2018, including terminating the SHERBOC clinical trial. The decision to terminate the SHERLOC clinical trial was made based on an interim analysis triggered by the occurrence of 75% of events required for trial completion, which demonstrated that the addition of MM-121 to docetaxel did not improve progression free survival over docetaxel alone in this patient population.

Also, in November 2018, we announced an amendment to our Phase 1 clinical trial of MM-310 to extend the dosing interval of MM-310 from every three weeks to every four weeks.

Also, in June 2018, we announced top-line results from the CARRIE clinical trial, showing that the trial did not meet its primary or secondary efficacy endpoints in patients who received MM-141 in combination with nab-paclitaxel and gemcitabine, compared to nab-paclitaxel and gemcitabine alone. These results were consistent in all subgroups analyzed. Based on these results, we are not devoting additional resources to and have ceased all of our development activities for MM-141.

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

We may never receive approval to commercialize our product candidates in the United States or other jurisdictions. Before obtaining regulatory approval for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more of our clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and successful interim results of a clinical trial do not necessarily predict successful final results.

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

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be insufficient or slower than we anticipate or patients may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
-

we might have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding of a lack of clinical response or a finding that the patients are being exposed to unacceptable health risks;

- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;
- the cost of clinical trials of our product candidates may be greater than we anticipate;

- the supply or quality of our product candidates, companion diagnostics or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate or prohibitively expensive; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators to suspend or terminate the trials.

For example, in November 2018, we announced that we are discontinuing development of all ongoing MM-121 programs based on the results of the interim analysis of the SHERLOC clinical trial that were announced on October 19, 2018, including terminating the SHERBOC clinical trial. The decision to terminate the SHERLOC clinical trial was made based on an interim analysis triggered by the occurrence of 75% of events required for trial completion, which demonstrated that the addition of MM-121 to docetaxel did not improve progression free survival over docetaxel alone in this patient population.

Also, in November 2018, we announced an amendment to our Phase 1 clinical trial of MM-310 to extend the dosing interval of MM-310 from every three weeks to every four weeks. Although early data from the clinical trial from the every three week dosing schedule regimen showed signs of encouraging antitumor activity in four patients, emerging cumulative grade 3 peripheral neuropathy following multiple cycles of treatment was observed in three patients. Pharmacokinetic and preclinical data indicate that lengthening the time between dosing may improve the tolerability of MM-310.

In addition, in June 2018, we announced top-line results from the CARRIE clinical trial, showing that the trial did not meet its primary or secondary efficacy endpoints in patients who received MM-141 in combination with nab-paclitaxel and gemcitabine, compared to nab-paclitaxel and gemcitabine alone.

Preclinical and clinical data may not be predictive of the success of later clinical trials, and are often susceptible to varying interpretations and analyses. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

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

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

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

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

If serious adverse or undesirable side effects are identified during the development of our product candidates or following their approval and commercialization, we may need to modify or abandon our development or marketing of such product or product candidate.

All of our product candidates are still in preclinical or clinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval, and it is impossible to ensure that safety or efficacy issues will not arise following regulatory approval. Currently marketed therapies for solid tumors are generally limited to some extent by their toxicity. Use of our product candidates as monotherapies in clinical trials also has resulted in adverse events consistent in nature with other marketed therapies. When used in combination with other marketed or investigational therapies, our product candidates may exacerbate adverse events associated with the other therapy. If our products or product candidates, either alone or in combination with other therapies, result in undesirable side effects or have characteristics that are unexpected, we may need to modify or abandon their development or marketing.

If we experience delays in the enrollment of patients in our clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to obtain a statistically significant result as required by the FDA or other regulatory authorities. In addition, many of our competitors have ongoing clinical trials for product candidates that could be competitive with our product candidates. Patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates or rely upon treatment with existing therapies that may preclude them from eligibility for our clinical trials.

Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of the company to decline and limit our ability to obtain additional financing. Our inability to enroll a sufficient number of patients for any of our current or future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

In general, we forecast enrollment for our clinical trials based on experience from previous clinical trials and monitor enrollment to be able to make adjustments to clinical trials when appropriate, including as a result of slower than expected enrollment that we experience from time to time in our clinical trials. It is possible that slow enrollment could require us to make adjustments to our clinical trials. If these adjustments do not overcome problems with slow enrollment, we could experience significant delays or abandon the applicable clinical trial altogether.

If we are unable to successfully develop companion diagnostics for our product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our product candidates.

An important component of our business strategy is to develop, either alone or together with third parties, companion diagnostics for each of our product candidates. There has been limited success to date industry-wide in developing companion diagnostics. To be successful, we will need to address a number of scientific, technical, regulatory and logistical challenges.

All of our companion diagnostic candidates are in preclinical or clinical development. We have limited experience in the development of companion diagnostics and may not be successful in developing appropriate diagnostics to pair with any of our product candidates that receive marketing approval. The FDA and similar regulatory authorities outside the United States are generally expected to regulate in vitro companion diagnostics as medical devices and to require separate regulatory approval prior to commercialization. Given our limited experience in developing diagnostics, we expect to rely in part on third parties for their design, development and manufacture. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics for our product candidates, or experience delays in doing so, the development of our product candidates may be adversely affected, our product candidates may not receive marketing approval and we may not realize the full commercial potential of any product candidates that receive marketing approval. As a result, our business would be harmed, possibly materially.

Any of our product candidates that receive regulatory approval may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Even if any of our product candidates receive marketing approval, they may nonetheless not gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors that may be uncertain or subjective, including:

- the prevalence and severity of any side effects;
- efficacy and potential advantages or disadvantages compared to alternative treatments;
- the price we charge for our product candidates;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- our ability to successfully develop companion diagnostics that effectively identify patient populations likely to benefit from treatment with our product candidates;
- the strength of marketing and distribution support; and
- sufficient third-party coverage or reimbursement.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new therapeutic and diagnostic products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any products that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Several large pharmaceutical and biotechnology companies currently market and sell products for the treatment of the solid tumor indications for which we are developing our product candidates. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization. Many of these competitors are attempting to develop therapeutics for our target indications.

We are developing our product candidates for the treatment of solid tumors. There are a variety of available therapies marketed for solid tumors. In many cases, these drugs are administered in combination to enhance efficacy. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs 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.

There are also a number of products in late stage clinical development to treat solid tumors. Our competitors may develop products that are more effective, safer, 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. In addition, our ability to compete may be affected because in many cases insurers or other third-party payors seek to encourage the use of generic products. There are many generic products currently on the market for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products 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 third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

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

The regulations that govern marketing approvals, pricing and reimbursement for new therapeutic and diagnostic products vary widely from country to country. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product

candidates obtain regulatory approval.

Our ability to commercialize any approved products successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors, including government payors such as Medicare and Medicaid, private health insurers and managed care organizations. There have been, and we expect there will continue to be, legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell our products profitably. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. The federal government, state legislatures and foreign governments 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 requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals and the other product candidates that we are developing and could have a material adverse effect our net revenue and results.

Third-party payors decide which drugs they will pay for and establish reimbursement and co-pay levels. The growing emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Third-party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. In order to secure 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 the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Even with clinical trials, our product candidates may be considered less safe, less effective or less cost-effective than other products, and third-party payors may not provide coverage and reimbursement for our products or any of our product candidates that we commercialize, in whole or in part.

The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on a formulary, which might not include all of the approved drugs for a particular indication, and a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved.

We cannot be sure that reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Reimbursement may impact the demand for, or the price of, any product for which we obtain marketing approval. Third-party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with products administered under the supervision of a physician. In addition, coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. Thus, 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. The marketability of any products for which we receive regulatory approval for commercial sale may also suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

Moreover, there may be significant delays in obtaining reimbursement for any approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries. Eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed, and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future weakening of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and appropriate payment rates from both government-funded and private payors for new products that we develop could therefore have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and an even greater risk related to the commercial sale of any products that we may develop. If we cannot successfully defend ourselves against claims that any of our product candidates caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for the products or product candidates that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of patients from clinical trials;
- significant costs to defend the related litigation;

- substantial monetary awards to patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.

We currently hold $10.0 million in product liability insurance coverage, which may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any or every liability that may arise.

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 research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or 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.

We also may not be successful in our efforts to identify or discover new or additional product candidates beyond our current preclinical and clinical product candidates. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development.

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 otherwise been more advantageous for us to retain sole development and commercialization rights.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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

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

Fluctuations in foreign currency exchange rates could substantially increase the costs of our clinical trial programs.

A significant portion of our clinical trial activities have historically been conducted outside of the United States, and associated costs may be incurred in the local currency of the country in which the trial is being conducted, which costs could be subject to fluctuations in foreign exchange rates. At present, we do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the U.S. dollar. A decline in the value of the U.S. dollar against currencies in geographies in which we conduct clinical trials could have a negative impact on our research and development costs. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our development costs.

Risks Related to Our Dependence on Third Parties

We may depend on collaborations with third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

Depending on our capital requirements, development and commercialization costs, need for additional therapeutic expertise and other factors, it is possible that we will enter into additional development and commercialization arrangements with respect to either oncology product candidates or product candidates in other therapeutic areas.

Our potential collaborators for any distribution, marketing, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We will have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between us and the collaborators that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated, such as the termination of our license and collaboration agreement with Sanofi effective December 17, 2014, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

For instance, although it is not a collaboration agreement, Ipsen has agreed pursuant to the asset sale agreement to use commercially reasonable efforts to develop ONIVYDE in connection with obtaining the regulatory approval by the FDA of ONIVYDE for certain indications. Although the results of this approval process may enable Ipsen to achieve the milestones necessary for us to receive the contingent payments under the asset sale agreement, there is no guarantee that Ipsen will take the steps set forth in the asset sale agreement and that such development will lead to the successful approval of ONIVYDE for such additional indications. Therefore, there can be no guarantees that any of the milestones set forth in the asset sale agreement will be achieved and that we will receive any future contingent payments.

Additionally, although the asset sale agreement entitles us to receive certain net milestone payments of up to $33.0 million that may become payable under the Servier agreement, to date we have received only $28.0 million of such net milestone payments. Payment of the remaining $5.0 million is not guaranteed for the milestone related to the first patient dosed in a pivotal clinical trial of ONIVYDE in an indication other than pancreatic cancer, as the satisfaction of such milestone is based on a clinical trial being conducted by Ipsen and Servier and is therefore out of our control.

If we are not able to establish additional collaborations, we may have to alter our development plans.

Our product development programs and the potential commercialization of any approved product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

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. We may not be able to negotiate collaborations on acceptable terms, or at all. If that were to occur, we may have to curtail the development of a particular product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of our sales or marketing activities, 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.

We rely 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 contract research organizations, clinical data management organizations, medical institutions and clinical investigators, 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, the FDA and other international regulatory agencies require us to comply with standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that adverse event data are reported within required timeframes, that data and reported results are credible and accurate and that the rights, integrity and confidentiality of patients in clinical trials are protected. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

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

We also intend to utilize companion diagnostics in several of our current and planned clinical trials, including our current clinical trial of MM-310, to preselect patients who will receive specified treatment regimens. We will rely on

third-party laboratories to test patient samples in connection with such companion diagnostics. Any failure on the part of these laboratories to properly perform such testing could jeopardize those clinical trials and delay or prevent the approval of the associated product candidate.

Risks Related to the Manufacturing of Our Product Candidates

We rely on third parties for the production of our product candidates. This increases the risk that we will not have sufficient quantities of our product candidates at an acceptable cost or on an acceptable schedule, which could delay, prevent or impair our development or commercialization efforts.

We rely on third-party manufacturers for most of the aspects of the production of our product candidates, including the production of bulk drug substance and fill finish and labeling activities. Although we are discussing arrangements for the manufacture of our product candidates with third parties, we do not currently have agreements for such arrangements in place and may be unable to conclude such agreements or to do so on acceptable terms. Reliance on third-party manufacturers entails risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, or Quality System Regulation, or QSR, 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 product candidates.

For instance, in 2010, a former fill finish third-party contractor that we used to fill and package MM-121 experienced FDA inspection issues with its quality control processes that resulted in a formal warning letter from the FDA. As a result, we pulled some MM-121 from clinical trial sites and replaced it with MM-121 that was filled by a different contractor. This restocking resulted in a few patients missing one or two doses of MM-121. It is possible that we could experience similar issues with other contractors.

Furthermore, our products may compete with the products of other companies for access to manufacturing facilities. Because there are a limited number of manufacturers that operate under cGMP or QSR regulations and that might be capable of manufacturing for us at an appropriate scale, we may not have access to such manufacturers.

We also rely on certain single suppliers for certain materials that we use for the manufacture of our product candidates. We purchase these materials from our suppliers on a purchase order basis and do not have long-term supply agreements in place. 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 may be 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 also rely upon third-party manufacturers to provide us with necessary reagents and instruments to develop, test and manufacture our in vitro diagnostics.

Our dependence upon others for the manufacture of our product candidates and companion diagnostics may adversely affect our future profit margins and our ability to commercialize any products that receive regulatory approval on a timely and competitive basis.

Risks Related to Our Intellectual Property

If we fail to fulfill our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements with third parties, including with respect to MM-310, and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that our future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate these agreements, in which event we might not be able to develop and market any product that is covered by these agreements. Termination of these licenses or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms. The occurrence of such events could materially harm our business.

If we are unable to obtain and maintain patent protection for our technology and products, or if our licensors are unable to obtain and maintain patent protection for the technology or products that we license from them, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be adversely affected.

Our success depends in large part on our and our licensors' ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or products that we license from third parties. Therefore, 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. In addition, if third parties who license patents to us fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and products that are important to our business. This 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.

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 and our licensors' patent rights are highly uncertain. Our and our licensors' pending and future patent applications may not result in patents being issued that protect our technology or products or that effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may 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. 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 or our licensors were the first to make the inventions claimed in our owned and licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions. Assuming the other requirements for patentability are met, the first to file a patent application is entitled to the patent. Under the America Invents Act enacted in 2011, the United States moved to this first to file system in 2013 from the previous system under which the first to make the claimed invention was entitled to the patent. We may become involved in opposition, interference or derivation proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such proceeding 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 products without infringing third-party patent rights.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed 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 scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. 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 owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Competitors may infringe our patents. To counter infringement or unauthorized use, we may be required to initiate infringement lawsuits, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, 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. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our products and product candidates and use our proprietary technologies without infringing the enforceable proprietary rights of third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties can have a similar negative impact on our business.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees 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 do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. 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. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

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

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

In addition to our patented technology and products, we rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties that have access to them, such as our employees, corporate collaborators, outside scientific collaborators, sponsored researchers, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Any of these parties may breach these agreements and disclose our proprietary information, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, 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 were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We may not be able to obtain, maintain or protect proprietary rights necessary for the continued development and commercialization of our products, product candidates and research technologies, including as a result of challenges from companies who seek to sell generic or biosimilar versions of our products after expiration of any regulatory exclusivity but prior to the applicable patent expiration.

Our commercial success depends in large part on obtaining and maintaining U.S. and foreign patent protection for our products, our product candidates and our research technologies and successfully enforcing and defending these patents against third-party challenges, including with respect to generic or biosimilar challenges. The validity of our patents in one or more jurisdictions may be challenged by third parties, resulting in our patents being deemed invalid, unenforceable or narrowed in scope, which could compromise the scope or duration of our exclusive rights in the relevant product, product candidate or technology. For example, the validity of a U.S. patent can be challenged in the U.S. Patent and Trademark Office (e.g., through an Inter Partes Review and/or Post Grant Review proceeding) and/or in U.S. federal district court.

In addition, our patents may also be challenged in a federal court in connection with a third party’s abbreviated new drug application, or ANDA, a Section 505(b)(2) new drug application, or NDA, or a Biologic License Application under Section 351(k), or BLA, seeking FDA approval to market a generic version or a biosimilar version of our products, resulting in a patent challenge to one or more patents listed in the Orange Book for our product or that protect our biologic product. This patent challenge can result in one or more of those patents for our products being deemed uninfringed, invalid, unenforceable and/or narrowed in scope, which could compromise the scope or duration of our exclusive rights in the relevant product. An ANDA, Section 505(b)(2) NDA or BLA can be filed after FDA approval of a product and the expiration of any relevant regulatory exclusivity. Other challenges to a patent may be mounted without regard to the date of an FDA approval.

Our patents as issued or as subsequently limited by any litigation might not contain claims that are sufficiently broad to prevent others from circumventing our patent protection and utilizing our technologies. For instance, the issued patents relating to our product candidates may be limited to a particular indication and/or composition and may not cover similar compositions that have similar clinical properties. Consequently, our competitors may independently develop competing products that do not infringe our patents or other intellectual property. Also, our pending patent applications may not issue, and we may not receive any additional patents. We cannot be sure that our patents and patent applications, including our own and those that we have rights to under licenses from third parties, will adequately protect our intellectual property for a number of reasons, including, among other things, the following: (i) the patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions; (ii) the actual protection afforded by a patent can vary from country to country and may depend upon the type of patent, the scope of its coverage and the availability of legal remedies in the country; (iii) the laws of foreign countries in which we market our products may afford little or no effective protection to our intellectual property, thereby easing our competitors' ability to compete with us in such countries; (iv) intellectual property laws and regulations and legal standards relating to the validity, scope and enforcement of patents covering pharmaceutical and biotechnological inventions are continually developing and changing, both in the United States and in other important markets outside the United States; (v) third parties may challenge, infringe, circumvent or seek to invalidate existing or future patents owned by or licensed to us; and (vi) the coverage claimed in a patent application can be significantly reduced before the patent is issued, and, as a consequence, our and our partners' patent applications may result in patents with narrower coverage than we desire or have planned for.

Risks Related to Regulatory Approval of Our Product Candidates

If we are not able to obtain required regulatory approvals, we will not be able to commercialize our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, import, export, sampling and marketing are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain regulatory approval for a product candidate will prevent us from commercializing the product candidate. ONIVYDE was our first and only product candidate to receive regulatory approval, and so we have only limited experience in filing and supporting the applications necessary to gain regulatory approvals. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA and other regulatory agencies for each therapeutic indication to establish the product candidate’s safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA or other regulatory agencies. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining regulatory approval or prevent or limit commercial use.

The process of obtaining regulatory approvals is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based on a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in regulatory approval policies during the development period, changes in or the enactment of additional statutes or regulations, changes in regulatory review for each submitted product application or approval of other products for the same indication may cause delays in the approval or rejection of an application. Regulatory agencies have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of a product candidate. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we continue to pursue development of companion diagnostics to identify patients who are likely to benefit from our product candidates, failure to obtain approval for the companion diagnostic may prevent or delay approval of the product candidate.

We are attempting to develop companion diagnostics to identify patients who are likely to benefit from our product candidates. We currently rely on and expect to continue to rely on third parties for much of the development, testing and manufacturing of our companion diagnostics. We will likely rely on such third parties to also obtain any required regulatory approval for and then commercially supply such companion diagnostics. All of our companion diagnostic candidates are in preclinical development or clinical feasibility testing. We have very limited experience in the development of diagnostics and, even with the help of third parties with greater experience, may fail to obtain the required diagnostic product marketing approval, which could prevent or delay approval of the product candidate.

In July 2014, the FDA issued final guidance that stated that if safe and effective use of a therapeutic depends on an in vitro diagnostic, then the FDA generally will not approve the therapeutic unless the FDA approves or clears this “in vitro companion diagnostic device” at the same time that the FDA approves the therapeutic. The approval or clearance of the in vitro diagnostic most likely will occur through the FDA’s Center for Devices and Radiological Health Office of In Vitro Diagnostics and Radiological Health. Even with the issuance of the final guidance, the FDA’s expectations for in vitro companion diagnostics remain unclear in some respects. The FDA’s developing expectations will affect our in vitro companion diagnostics. In particular, the FDA may limit our ability to use retrospective data, otherwise disagree with our approaches to trial design, biomarker qualification, clinical and analytical validity and clinical utility, or make us repeat aspects of the trial or initiate new trials.

Because our companion diagnostic candidates are at an early stage of development, we cannot yet know what the FDA will require for any of these tests. For MM-310, we are attempting to develop an in vitro companion diagnostic that will help identify patients likely to benefit from the therapy. Whether the FDA will consider this in vitro diagnostic to be an “in vitro companion diagnostic device” that requires simultaneous approval or clearance with the therapeutic will depend on whether the FDA views the diagnostic to be essential to the safety and efficacy of MM-310.

Based on the FDA’s past practice with companion diagnostics, if we are successful in developing a diagnostic for MM-310 or any of our future clinical stage product candidates, we would expect that FDA approval of an in vitro companion diagnostic would be required for approval and subsequent commercialization of each such product candidate. We are not aware of any currently available diagnostics that, if necessary, would otherwise allow us to proceed with the approval and subsequent commercialization of our product candidates despite a delay in or failure of our attempts to develop diagnostics.

Because we expect to rely on third parties for various aspects of the development, testing and manufacture, as well as for regulatory approval for and commercial supply, of our companion diagnostics, the commercial success of any of our product candidates that require a diagnostic will be tied to and dependent on the continued ability of such third parties to make the diagnostic commercially available on reasonable terms in the relevant geographies.

If we fail to obtain or maintain orphan drug designation for any of our product candidates, we will have to rely on other rights and protections.

In the United States, under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

In the United States, the company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for that indication for a period of seven years. This orphan drug exclusivity prevents the FDA from approving another application, including a full NDA, to market the same drug for the same orphan indication, except in limited circumstances. For purposes of small molecule drugs, the FDA defines the term “same drug” to mean a drug that contains the same active molecule and that is intended for the same use as the approved orphan drug. Orphan drug exclusivity may be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Additionally, maintenance of the orphan drug designation requires the company holding such designation to continue to actively pursue development in that indication.

None of our product candidates currently in active development have obtained orphan drug designation. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA’s pre-existing regulatory interpretation to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any such changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Our product candidates for which we intend to seek approval as biological or drug products may face competition sooner than expected.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as part of the Health Care and Education Reconciliation Act of 2010, or the Health Care Reform Laws, an abbreviated pathway for the approval of biosimilar and interchangeable biological products was created. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as “interchangeable” based on their similarity to existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until twelve years after the original branded product was approved under a biologics license application, or BLA. The BPCIA is complex and has yet to be fully interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning is subject to uncertainty. While it is uncertain when any such processes 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 products approved as a biological product under a BLA should qualify for the twelve year period of exclusivity. However:

- a potential competitor could seek and obtain approval of its own BLA during our exclusivity period instead of seeking approval of a biosimilar version; and
- the FDA could consider a particular product candidate which contains both drug and biological product components to be a drug subject to review pursuant to an NDA, and therefore eligible for a significantly shorter marketing exclusivity period as provided under the Drug Price Competition and Patent Term Restoration Act of 1984.

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.

In addition, a drug product approved under an NDA could face generic competition earlier than expected. The enactment of the Generic Drug User Fee Amendments of 2012 as part of the Food and Drug Administration Safety and Innovation Act of 2012 established a user fee program that will generate hundreds of millions of dollars in funding for the FDA's generic drug review program. Funding from the user fee program, along with performance goals that the FDA negotiated with the generic drug industry, is significantly decreasing the timeframe for FDA review and approval of generic drug applications.

Failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our products abroad.

We intend to market any product for which we obtain marketing approval, either ourselves or with commercialization partners, both within and outside the United States. This may increase the risks described below with respect to our compliance with foreign regulations.

In order to market and sell any approved products in the European Union and many other jurisdictions, we or our commercialization partners must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing, including sometimes additional testing in children. The time required to obtain approval in foreign countries may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be sold in that country. We or our future commercialization partners may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We or our future commercialization partners may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals as a result of Brexit or otherwise would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

Any product for which we obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product for which we may obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP or QSR requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if regulatory approval of a product is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. Later discovery of previously unknown problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in actions such as:

- restrictions on such products, manufacturers or manufacturing processes;

- restrictions on the marketing of a product;
- restrictions on product distribution;
- requirements to conduct post-marketing clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

The FDA has sweeping inspection authorities to enforce the Federal Food, Drug, and Cosmetic Act. Under the statute, a drug or biologic will be considered adulterated, with possible resulting civil and criminal penalties, if the owner or operator of the establishment where it is made, processed, packed or held delays, denies, limits or refuses inspection. The FDA employs a risk-based inspection schedule to ensure compliance. The law grants the FDA authority to require a drug or biologics manufacturer to provide, in advance or instead of an inspection, and at the manufacturer's expense, any records or other information that the agency may otherwise inspect at the facility. The FDA may also share inspection information with foreign governments under certain circumstances.

The FDA also has broad authority to take action against manufacturers of drugs or biologics that are not adhering to pediatric study requirements, which apply even if the manufacturer is not seeking to market the drug or biologic to pediatric patients. As of April 2013, the FDA must issue non-compliance letters to companies who do not meet the pediatric study requirements. Any company receiving a non-compliance letter would have an opportunity to respond, and the non-compliance letter and company response would become publicly available.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been and continue to be a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010, the Health Care Reform Laws were enacted, which include measures that have significantly changed healthcare financing by both governmental and private insurers. Since enactment of the Health Care Reform Laws, there have been numerous legal challenges and legislative actions to repeal and replace provisions of the law, and we expect these to continue. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, the U.S. Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the U.S. 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. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Health Care Reform Law-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share and the medical device excise tax on non-exempt medical devices.

The U.S. Congress may consider other legislation to replace elements of the Health Care Reform Laws during the next Congressional session. These healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to product pricing, review the relationship

between pricing and manufacturer patient programs, reduce the costs of products under Medicare and reform government program reimbursement methodologies for products. At the federal level, the U.S. Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription product and other healthcare programs. These measures could reduce the ultimate demand for our product candidates, once approved, or put pressure on our product pricing.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent product labeling and post-marketing testing and other requirements.

Risks Related to Commercialization of Our Product Candidates

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. If we are found to have improperly promoted off-label uses for any product for which we receive marking approval, we may become subject to significant fines and other liability.

The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we are found to have promoted for off-label uses, we may become subject to significant government fines and other related liability. For example, the U.S. government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The government has also required companies to enter into complex multi-year corporate integrity agreements and/or non-prosecution agreements that can impose significant restrictions and other burdens on the affected companies.

In addition, incentives under applicable U.S. laws encourage employees and physicians to report violations of rules governing promotional activities for pharmaceutical products. These incentives could lead to so called whistleblower lawsuits as part of which such persons seek to collect a portion of moneys allegedly overbilled to government agencies due to, for example, promotion of pharmaceutical products beyond labeled claims. Such lawsuits, whether with or without merit, are typically time consuming and costly to defend. Such suits may also result in related stockholder lawsuits, which are also costly to defend.

Our relationships with customers and payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others play a primary role in the recommendation and prescription of products for which we obtain marketing approval. Arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal, state and foreign healthcare laws and regulations include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward the purchasing, leasing, ordering or arranging for the purchase, order or recommendation of any item or service reimbursable under Medicare, Medicaid, or other federal healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other, and violations are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to

induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor;

- the federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Government enforcement agencies and private whistleblowers have initiated investigations or brought private lawsuits against pharmaceutical companies for a variety of allegedly improper promotional or marketing activities, such as allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates; allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product; or engaging in promotion for "off-label" uses. Additionally, the Health Care Reform Laws amended the federal False Claims Act such that a violation of the federal anti-kickback statute can serve as a basis for liability under the False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, or HIPAA, makes it a crime to knowingly and willfully execute or attempt to execute a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits, among other things, knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Health Care Reform Laws require manufacturers of drugs, devices, biologics and medical supplies reimbursable under Medicare and Medicaid to report to the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals, as well as physician ownership and investment interests, and provide for public reporting of the data reported by manufacturers;
- the U.S. Foreign Corrupt Practices Act prohibits U.S. companies and their representatives from paying, offering to pay, promising or authorizing the payment of anything of value to any foreign government official, government staff member, political party or political candidate for the purpose of obtaining or retaining business or to otherwise obtain favorable treatment or influence a person working in an official capacity, and encompasses many healthcare professionals in many countries under the definition of a foreign government official;
- the Bribery Act, which applies to U.S. companies such as ourselves that conduct business in the United Kingdom, proscribes giving and receiving bribes in the public and private sectors, bribing a foreign public official and failing to have adequate procedures to prevent employees and other agents from giving bribes; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers. In addition, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government. Other states require pharmaceutical manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures, or prohibit certain marketing-related activities including the provision of gifts, meals or other items to certain healthcare providers.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could also harm our financial condition. Responding to government investigations or whistleblower lawsuits, defending any claims raised, and any resulting fines, damages, penalties, settlement payments or administrative actions, as well as any related actions brought by stockholders or other third parties, could have a material impact on our reputation, business and financial condition and divert the attention of our management from operating our business.

Our corporate compliance efforts cannot guarantee that we are in compliance with all potentially applicable regulations.

The development, manufacturing, pricing, sales, coverage and reimbursement of our products, together with our general operations, are and will be subject to extensive regulation by federal, state and other authorities within the

United States and numerous entities outside of the United States. While we have implemented a corporate compliance program based on what we believe are the current best practices, we cannot provide any assurance that governmental authorities will find that our business practices comply with current or future administrative or judicial interpretations of potentially applicable laws and regulations. If we fail to comply with any of these laws and regulations, we could be subject to a range of regulatory actions, including suspension or termination of clinical trials, the failure to approve a product candidate, restrictions on our products or manufacturing processes, withdrawal of products from the market, significant fines, disqualification or debarment from participation in federally-funded healthcare programs or other sanctions or litigation, any of which events may have a significant adverse impact on our business.

Risks Related to Data Protection and Cybersecurity

Our failure to comply with data protection laws and regulations could lead to government enforcement actions, private litigation and/or adverse publicity and could negatively affect our operating results and business.

We are subject to data protection laws and regulations that address privacy and data security. The legislative and regulatory landscape for data protection continues to evolve, and in recent years there has been an increasing focus on privacy and data security issues. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws and federal and state consumer protection laws govern the collection, use, disclosure and protection of health-related and other personal information. Failure to comply with data protection laws and regulations could result in government enforcement actions, which could include civil or criminal penalties, private litigation and/or adverse publicity and could negatively affect our operating results and business. In addition, we may obtain health information from third parties (e.g., healthcare providers who prescribe our products) that are subject to privacy and security requirements under HIPAA. We could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information in a manner that is not authorized or permitted.

The collection and use of personal health data in the European Union is governed by the provisions of the General Data Protection Regulation, or GDPR, which came into effect in May 2018. This regulation imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the GDPR and the related national data protection laws of the European Union Member States may result in significant fines and other administrative penalties.

Significant disruptions of information technology systems or security breaches could adversely affect our business.

We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit large amounts of confidential information (including, among other things, trade secrets or other intellectual property, proprietary business information and personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We also have outsourced elements of our operations to third parties, and as a result we manage a number of third-party vendors who may or could have access to our confidential information. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, and the large amounts of confidential information stored on those systems, make such systems vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors, and/or business partners, or from cyber-attacks by malicious third parties. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks could also include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

Significant disruptions of our information technology systems, or those of our third-party vendors, or security breaches could adversely affect our business operations and/or result in the loss, misappropriation and/or unauthorized access, use or disclosure of, or the prevention of access to, confidential information, including, among other things, trade secrets or other intellectual property, proprietary business information and personal information, and could result in financial, legal, business and reputational harm to us. For example, any such event that leads to unauthorized

access, use or disclosure of personal information, including personal information regarding our patients or employees, could harm our reputation, require us to comply with federal and/or state breach notification laws and foreign law equivalents, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. Security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures to protect our information technology systems and infrastructure, there can be no assurance that such measures will prevent service interruptions or security breaches that could adversely affect our business.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the principal members of our executive and scientific teams. Although we have formal employment agreements with each of our executive officers, these agreements do not prevent our executives from terminating their employment with us at any time. We do not maintain “key person” insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

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 that may limit their availability to us.

Our corporate restructuring and the associated headcount reduction announced in November 2018 may not result in anticipated savings, could result in total costs and expenses that are greater than expected and could disrupt our business.

On November 7, 2018, we announced that we were implementing a reduction in headcount as part of a corporate restructuring, after which we expected to have approximately 27 employees. We may not realize, in full or in part, the anticipated benefits, savings and improvements in our cost structure from our restructuring efforts due to unforeseen difficulties, delays or unexpected costs. If we are unable to realize the expected operational efficiencies and cost savings from the restructuring, our operating results and financial condition would be adversely affected. We also cannot guarantee that we will not have to undertake additional headcount reductions or restructuring activities in the future. Furthermore, our restructuring plan may be disruptive to our operations. For example, our headcount reductions could yield unanticipated consequences, such as attrition beyond planned staff reductions, or increase difficulties in our day-to-day operations. Our headcount reductions could also harm our ability to attract and retain qualified personnel who are critical to our business, which in turn could prevent us from successfully developing and commercializing our product candidates in the future.

We have entered into and may continue to enter into or seek to enter into business combinations, acquisitions or divestitures which may be difficult to consummate, disrupt our business, divert management attention or dilute stockholder value.

As part of our business strategy, we may enter into business combinations, acquisitions or divestitures. Although we consummated the asset sale to Ipsen in April 2017, we have limited experience in making acquisitions and divestitures. In addition, acquisitions and divestitures are typically accompanied by a number of risks, including:

- the difficulty of integrating or separating the operations and personnel of the acquired companies or divested product;
- the potential disruption of our ongoing business and distraction of management;
- potential unknown liabilities and expenses;
- the failure to achieve the expected benefits of the combination, acquisition or divestiture;
- the maintenance of acceptable standards, controls, procedures and policies; and
- the impairment of relationships with employees as a result of any integration or separation of management and other personnel.

If we are not successful in completing acquisitions or divestitures that we may pursue in the future, we would be required to reevaluate our business strategy and we may have incurred substantial expenses and devoted significant management time and resources in seeking to complete the acquisitions or divestitures. In addition, with future acquisitions, we could use substantial portions of our available cash as all or a portion of the purchase price or could issue additional securities as consideration for these acquisitions, which could cause our stockholders to suffer significant dilution.

Risks Related to Our Common Stock

Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock, in the aggregate, beneficially own a large portion of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could discourage, delay or prevent an acquisition of our company on terms that other stockholders may desire.

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

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. Among others, these provisions:

- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our stock price has been and may in the future be volatile, which could cause holders of our common stock to incur substantial losses.

Our stock price has been and in the future may be subject to substantial price volatility. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders could incur substantial losses. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patents or other proprietary rights;
- the recruitment or departure of key personnel;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors and issuance of new or changed securities analysts’ reports or recommendations;
- activism by any single large stockholder or combination of stockholders;

- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

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

We have not historically declared or paid regular cash dividends on our common stock. Although our board of directors declared a special cash dividend of $140.0 million, which was payable on May 26, 2017 to stockholders of record as of the close of business on May 17, 2017, we do not currently intend to pay any regular cash dividends in the foreseeable future. In addition, the terms of the Loan Agreement with Hercules currently, and the terms of any future debt agreements may in the future, preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for holders of our common stock for the foreseeable future.

Future sales of shares of our common stock, including by us or our directors and executive officers, or shares issued upon the exercise of currently outstanding options could cause the market price of our common stock to drop significantly, even if our business is doing well.

A substantial portion of our outstanding common stock can be traded without restriction at any time. In addition, a portion of our outstanding common stock is currently restricted as a result of federal securities laws, but can be sold at any time subject to applicable volume limitations. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, by us or others, could reduce the market price of our common stock. In addition, we have a significant number of shares that are subject to outstanding options. The exercise of these options and the subsequent sale of the underlying common stock could cause a further decline in our stock price. For instance, in April 2016, we issued an aggregate of 1,236,766 shares of our common stock to certain holders of our convertible notes who had agreed to convert an aggregate of $64.2 million of convertible notes. Any such sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. We cannot predict the size of future issuances or the effect, if any, that any future issuances may have on the market price for our common stock.

Furthermore, on December 15, 2017, we filed a registration statement on Form S-3 with the SEC to allow the issuance of our securities from time to time in one or more offerings of up to $150,000,000 in aggregate dollar amount. This registration statement was declared effective by the SEC on January 5, 2018. Any sale of additional shares of our common stock or other securities could reduce the market price of our common stock.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our principal facilities consist of approximately 99,132 square feet of research and office space located at One Kendall Square in Cambridge, Massachusetts. The lease on our principal facilities expires in June 2019. In connection with the completion of the asset sale, on April 3, 2017, we entered into a sublease with Ipsen, pursuant to which Ipsen is subleasing approximately 64,550 square feet of space in our Cambridge, Massachusetts facility through the end of the term of the lease in June 2019.

Item 3. Legal Proceedings

We are not currently a party to any material 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

Our common stock is publicly traded on the Nasdaq Global Market under the symbol "MACK".

Holders

As of January 31, 2019, there were approximately 118 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

Although our board of directors declared a special cash dividend of $140.0 million, which was payable on May 26, 2017 to stockholders of record as of the close of business on May 17, 2017, we do not currently intend to pay any regular cash dividends in the foreseeable future, nor have we ever declared or paid any other cash dividends on our common stock.

Item 6. Selected Financial Data

We are not required to provide the information required by this Item because we are a smaller reporting company.

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

The following discussion of our financial condition and results of operations should be read in conjunction with our financial statements and the notes to those financial statements appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth in Part I, Item 1A. Risk Factors of this Annual Report on Form 10-K, which are incorporated herein by reference, our actual results may differ materially from those anticipated in these forward-looking statements.

Overview

We are a clinical stage biopharmaceutical company based in Cambridge, Massachusetts that is outthinking cancer by targeting biomarker-defined cancers. Our vision is to ensure that cancer patients and their families live fulfilling lives. Our mission is to transform cancer care through the smart design and development of targeted solutions based on a deep understanding of cancer pathways and biological markers. Our strategy is to (1) understand the biological problems we are trying to solve, (2) design specific solutions against the problems we are trying to solve and (3) develop those solutions for biomarker-selected patients. This three-pronged strategy seeks to ensure optimal patient outcomes. We own worldwide development and commercial rights to all of our clinical and preclinical programs.

On April 3, 2017, we began operating as a refocused research and clinical development company in connection with the completion of our previously announced transaction, or the asset sale, with Ipsen S.A., or Ipsen. Pursuant to the Asset Purchase and Sale Agreement, dated as of January 7, 2017, or the asset sale agreement, between us and Ipsen, Ipsen acquired our right, title and interest in the non-cash assets, equipment, inventory, contracts and intellectual property primarily related to or used in our business operations and activities involving or relating to developing, manufacturing and commercializing ONIVYDE, our first commercial product, and MM-436, or the commercial business. We received $575.0 million in cash, plus a working capital adjustment of $5.7 million, and are eligible to receive up to $450.0 million in additional regulatory approval-based milestone payments. We also retained the right to receive net milestone payments that may become payable for the ex-U.S. development and commercialization of ONIVYDE for up to $33.0 million pursuant to a license and collaboration agreement between Ipsen and Les Laboratoires Servier SAS, or Servier (as assignee from Shire plc), which we refer to as the Servier agreement. To date, we have received $28.0 million of the potential $33.0 million in milestone payments under the Servier agreement. We entered into the Servier agreement in 2014, and on April 3, 2017, the Servier agreement was assigned to Ipsen in connection with the completion of the asset sale. As a result of the asset sale, the commercial business is accounted for as a discontinued operation for all periods presented.

Our non-commercial assets, including our clinical and preclinical development programs, were not included in the asset sale and remain assets of ours.

Our only clinical stage asset in active development is MM-310. MM-310 is an antibody-directed nanotherapeutic that targets the ephrin receptor A2, or EphA2, receptor and contains a novel cytotoxic taxane. The EphA2 receptor is highly expressed in most solid tumor types, such as prostate, ovarian, bladder, gastric, pancreatic and lung cancers. We are conducting a Phase 1 clinical trial to evaluate safety and preliminary activity of MM-310 in patients with solid tumors and to identify the maximum tolerated dose.

Our two most promising preclinical programs are MM-401, an agonistic antibody targeting a novel immuno-oncology target, TNFR2, and MM-201, a highly stabilized agonist-Fc fusion protein targeting death receptors 4 and 5.

We have devoted substantially all of our resources to our drug discovery and development efforts, including conducting clinical trials for our product candidates, protecting our intellectual property and providing general and

administrative support for these operations. We currently have no products approved for sale and all of our revenue to date has been collaboration revenue and through sales of ONIVYDE and, to date, we have financed our operations primarily through private placements of convertible preferred stock, collaborations, public offerings of our securities, secured debt financings, sales of ONIVYDE and the asset sale.

On June 25, 2018, we announced top-line results from our global, double-blinded, placebo-controlled, Phase 2 randomized CARRIE clinical trial evaluating the addition of MM-141 (istiratumab) to standard-of-care treatment in patients with previously untreated metastatic pancreatic cancer and high serum levels of the insulin-like growth factor 1, or IGF-1. The CARRIE clinical trial did not meet its primary or secondary efficacy endpoints in patients who received MM-141 in combination with nab-paclitaxel and gemcitabine, compared to nab-paclitaxel and gemcitabine alone. These results were consistent in all subgroups analyzed. Based on these results, we are not devoting additional resources to and have ceased all of our development activities for MM-141.

On October 19, 2018, we announced the termination of our global, open-label, biomarker-selected, Phase 2 randomized SHERLOC clinical trial evaluating MM-121 (seribantumab) in combination with docetaxel in patients with heregulin positive non-small cell lung cancer, or NSCLC. The decision to terminate the SHERLOC clinical trial was made based on an interim analysis triggered by the occurrence of 75% of events required for trial completion, which demonstrated that the addition of MM-121 to docetaxel did not improve progression free survival over docetaxel alone in this patient population.

On November 7, 2018, based on the results of the interim analysis of the randomized Phase 2 SHERLOC clinical trial that were announced on October 19, 2018, we announced that we are discontinuing development of all ongoing MM-121 programs, including terminating the global, double-blinded, placebo-controlled, biomarker-selected, Phase 2 randomized SHERBOC clinical trial evaluating MM-121 in combination with fulvestrant in patients with heregulin positive, hormone receptor positive, ErbB2 (HER2) negative, metastatic breast cancer.

On November 7, 2018, we announced that we were implementing a reduction in headcount as part of a corporate restructuring, after which we expected to have approximately 27 employees. The corporate restructuring followed a comprehensive review of our drug candidate pipeline. The reduction in headcount was completed in February 2019.

In connection with the corporate restructuring, we also announced on November 7, 2018 that we have retained external advisors to explore strategic alternatives.

In October and November 2017, we paid approximately $59.1 million, including $0.7 million for accrued and unpaid interest and $3.8 million of transaction costs, to purchase all of the remaining $60.8 million aggregate principal amount of outstanding convertible notes. The Company paid, in cash, an amount equal to $900 per $1,000 principal amount of convertible notes purchased, plus accrued and unpaid interest to, but not including, the date of purchase. A loss on extinguishment was recognized in interest expense in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2017. The $0.3 million loss on extinguishment represents the difference between the total settlement consideration transferred to the holders that was attributed to the liability component of the convertible notes, based on the fair value of that component at the time of settlement, and the net carrying value of the liability. The remaining settlement consideration transferred was allocated to the reacquisition of the embedded conversion option and recognized as a $4.2 million reduction of additional paid-in capital. Transaction costs incurred with third parties related to the conversion were allocated to the liability and equity components and resulted in an additional $3.5 million of interest expense and a $0.3 million reduction on additional paid-in capital.

As of December 31, 2018, we had unrestricted cash and cash equivalents and marketable securities of $71.3 million. We believe that our financial resources as of December 31, 2018 and as a result of the corporate restructuring announced on November 7, 2018, together with other restructuring and cost cutting measures that we could implement in the future, provide us with the potential to fund our operations, including debt service obligations and capital expenditure requirements, into at least the second half of 2022.

We have never been profitable and, as of December 31, 2018, we had an accumulated deficit of $523.3 million. Our net loss from continuing operations was $60.8 million for the year ended December 31, 2018 and $76.0 million for the year ended December 31, 2017. As a result of the refocusing of our development efforts, as well as completing the closeout of our SHERLOC and SHERBOC clinical trials, we expect our research and development expenses to decrease in the year ending December 31, 2019 as compared to the year ended December 31, 2018. We will still incur research and development expenses for the foreseeable future as we continue to develop our product candidates and further advance our preclinical products and earlier stage research and development projects. Until such time, if ever, as we can generate sufficient product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, licensing arrangements and other marketing and distribution arrangements. We also could engage in discussions with third parties regarding partnerships, joint ventures, combinations or divestitures of one or more of our businesses as we seek to further the development of our research programs, improve our cash position and maximize stockholder value. There can be no assurance as to the timing, terms or consummation of any financing, collaboration, licensing arrangement or other marketing and distribution arrangement, partnership, joint venture, combination or divestiture. We may be unable to raise capital when needed or on attractive terms, which would force us to delay, limit, reduce or terminate our research and development programs. We will need to generate significant revenues to achieve profitability, and we may never do so.

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Strategic Partnerships, Licenses and Collaborations

Servier

On September 23, 2014, we entered into the Servier agreement for the development and commercialization of ONIVYDE outside of the United States and Taiwan, or the licensed territory. As part of the Servier agreement, we granted an exclusive, royalty-bearing right and license under our patent rights and know-how to develop and commercialize ONIVYDE in the licensed territory. On April 3, 2017, the Servier agreement and all other agreements related to the subject collaboration and any associated obligations, including our agreement related to commercial supply of ONIVYDE, were assigned to Ipsen in connection with the completion of the asset sale. We retained the rights to receive net milestone payments that may become payable pursuant to the Servier agreement for the ex-U.S. development and commercialization of ONIVYDE for up to $33.0 million, which is comprised of potential payments of $18.0 million from the sale of ONIVYDE in two additional major European countries, $5.0 million related to the sale of ONIVYDE in the first major non-European, non-Asian country and $10.0 million for the first patient dosed in a pivotal clinical trial in an indication other than pancreatic cancer. In October 2018, we received a payment of $5.0 million from Ipsen against the milestone related to the first patient dosed in a pivotal clinical trial of ONIVYDE in an indication other than pancreatic cancer as a result of the commencement of a multi-part study that Ipsen and Servier are conducting in patients with small-cell lung cancer. We expect to receive the remaining $5.0 million for such milestone if and when Ipsen and Servier decide to progress to the randomized part of the study focused on efficacy. To date, we have received $28.0 million of the potential $33.0 million in milestone payments under the Servier Agreement.

Actavis

In November 2013, we entered into a development, license and supply agreement with Watson Laboratories, Inc., or Actavis, which we refer to as the Actavis agreement, pursuant to which we agreed to develop, manufacture and exclusively supply the bulk form of doxorubicin hydrochloride (HCl) liposome injection, or the initial product, to Actavis. On April 3, 2017, in connection with the completion of the asset sale, the Actavis agreement was assigned to Ipsen.

Silver Creek Pharmaceuticals, Inc.

In August 2010, we acquired a controlling financial interest in Silver Creek, a research and development company focused on areas outside of oncology. At such time, we had the ability to direct the activities of Silver Creek that most significantly impacted Silver Creek's economic performance through our ownership percentage and through the board of director seats we controlled. As such, we initially consolidated Silver Creek.

In the third quarter of 2017, Silver Creek completed its Series C preferred stock financing, which reduced our ownership percentage in Silver Creek below 50% and resulted in us no longer controlling the Silver Creek board of directors. We determined that we were no longer the primary beneficiary of Silver Creek, as we do not control the board of directors and do not direct the activities that have the most significant impact on Silver Creek's economic performance. As a result, we deconsolidated Silver Creek from our financial statements on July 13, 2017 and we recorded a gain on the deconsolidation of Silver Creek of $10.8 million for the year ended December 31, 2017 in our consolidated statement of operations and comprehensive loss. Starting on July 14, 2017, we accounted for our investment in Silver Creek under the equity method of accounting as we have the ability to exercise significant influence over Silver Creek. The carrying value of our investment in Silver Creek was $7.4 million and $10.6 million at December 31, 2018 and 2017, respectively.

Financial Obligations Related to the License and Development of ONIVYDE

In September 2005, Hermes BioSciences, Inc., or Hermes, which we acquired in October 2009, entered into a license agreement with PharmaEngine, Inc., or PharmaEngine, under which PharmaEngine received an exclusive license to research, develop, manufacture and commercialize ONIVYDE in Europe and certain countries in Asia. In May 2011, we entered into a new agreement with PharmaEngine, which we refer to as the PharmaEngine agreement, under which we reacquired all previously licensed rights for ONIVYDE, other than rights to commercialize ONIVYDE in Taiwan. As a result, we had the exclusive right to commercialize ONIVYDE in all territories in the world, except for Taiwan, where PharmaEngine has an exclusive commercialization right.

On April 3, 2017, the PharmaEngine agreement and all related agreements and any associated obligations, including our agreement related to commercial supply of ONIVYDE to PharmaEngine, were assigned to Ipsen in connection with the asset sale.

Financial Operations Overview

Revenues

Our revenue through December 31, 2018 has been derived from license fees, milestone payments and research, development, manufacturing and other payments received from collaborations, as well as from sales of ONIVYDE.

As a result of the asset sale, all revenue related to the commercial business has been reclassified under discontinued operations.

In the future, we may generate revenue from a combination of research and development payments, license fees and other upfront payments, milestone payments, product sales and royalties in connection with any future collaborations and licenses. We expect that any revenue we generate will fluctuate in future periods as a result of the timing of our or a collaborator's achievement of preclinical, clinical, regulatory and commercialization milestones, if at all, the timing and amount of any payments to us relating to such milestones and the extent to which any of our product candidates are approved and successfully commercialized by us or a collaborator. If we fail, or any future collaborator fails, to develop product candidates in a timely manner or to obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Research and development expenses

Research and development expenses consist of the costs associated with our research and discovery activities, including investment in our systems biology approach, conduct of preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings. Our research and development expenses consist of:

- employee salaries and related expenses, which include stock-based compensation and benefits for the personnel involved in our drug discovery and development activities;
- external research and development expenses incurred under agreements with third-party contract research organizations and investigative sites;
- manufacturing material expense for third-party manufacturing organizations and consultants, including costs associated with manufacturing product prior to product approval;
- license fees for and milestone payments related to in-licensed products and technologies; and
- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment, and laboratory and other supplies.

We expense research and development costs as incurred. Conducting a significant amount of research and development is central to our business model. Product candidates in late stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of late stage clinical trials. As a result of the refocusing of our development efforts, as well as completing the closeout of our SHERLOC and SHERBOC clinical trials, we expect our research and development expenses to decrease in the year ending December 31, 2019 as compared to the year ended December 31, 2018. We will still incur research and development expenses for the foreseeable future as we continue to develop our product candidates and further advance our preclinical products and earlier stage research and development projects.

We use our employee and infrastructure resources across multiple research and development programs. We track expenses related to our most advanced product candidates on a per project basis. Accordingly, we allocate internal employee-related and infrastructure costs, as well as third-party costs, to each of these programs. We do not allocate to specific development programs either stock-based compensation expense or expenses related to preclinical programs. Costs that are not directly attributable to specific clinical programs, such as wages related to shared laboratory services, travel and employee training and development, are not allocated and are considered general research and

discovery expenses.

The following table summarizes our principal product development programs, including the research and development expenses allocated to each clinical stage product candidate, for the years ended December 31, 2018 and 2017:

	Years Ended December 31,	
(in thousands)	2018	2017
MM-121	$26,760	$14,082
MM-310	4,297	6,674
Legacy Programs	4,565	16,526
Preclinical, general research and discovery	13,259	23,130
Stock-based compensation	1,093	6,902
Total research and development expenses	$49,974	$67,314

In connection with the asset sale, all expenses related to the commercial business have been reclassified under discontinued operations.

The successful development of our clinical and preclinical product candidates is highly uncertain. At this time, other than as discussed below, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of any of our clinical or preclinical product candidates or the period, if any, in which material net cash flows from these product candidates may commence. This is due to the numerous risks and uncertainties associated with developing drugs, including the uncertainty of:

- the scope, rate of progress and expense of our ongoing, as well as any additional, clinical trials and other research and development activities;
- the potential benefits of our product candidates over other therapies;
- our ability to market, commercialize and achieve market acceptance for any of our product candidates that we are developing or may develop in the future;
- clinical trial results;
- the terms and timing of regulatory approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those which we currently anticipate will be required for the completion of clinical development of a product candidate or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

MM-121 (seribantumab)

In February 2015, we initiated the global, open-label, biomarker-selected, Phase 2 randomized SHERLOC clinical trial evaluating MM-121 in combination with docetaxel, versus docetaxel alone, in patients with heregulin positive NSCLC. On October 19, 2018, we announced the termination of the SHERLOC clinical trial based on an interim analysis triggered by the occurrence of 75% of events required for trial completion, which demonstrated that the addition of MM-121 to docetaxel did not improve progression free survival over docetaxel alone in this patient population.

In February 2018, we dosed the first patient in our global, double-blinded, placebo-controlled, biomarker-selected Phase 2 randomized SHERBOC clinical trial evaluating MM-121 in combination with fulvestrant, versus fulvestrant alone, in patients with heregulin positive, hormone receptor positive, ErbB2 (HER2) negative, metastatic breast cancer. On November 7, 2018, we announced that we are discontinuing development of all ongoing MM-121 programs, including terminating the SHERBOC clinical trial based on the results of the interim analysis of the SHERLOC clinical trial. We expect close out costs to continue through the first quarter of 2019.

MM-310

In March 2017, we initiated a Phase 1 clinical trial of MM-310 to evaluate its safety and preliminary activity in patients with solid tumors and to identify the maximum tolerated dose.

Legacy Programs

In January 2017, we announced the completion of our strategic pipeline review as a result of which many product candidates in our pipeline were put on hold until such time as we determine the conditions are appropriate to invest in them. These molecules include MM-302, MM-151, MM-131 and certain early stage discovery efforts.

In June 2018, we announced top-line results from the CARRIE clinical trial, showing that the trial did not meet its primary or secondary efficacy endpoints in patients who received MM-141 in combination with nab-paclitaxel and gemcitabine, compared to nab-paclitaxel and gemcitabine alone. Based on these results, we are not devoting additional resources to and have ceased all of our development activities for MM-141.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs for personnel, including stock-based compensation expenses and benefits, in our legal, intellectual property, business development, finance, information technology, corporate communications, investor relations and human resources departments. Other general and administrative expenses include costs for employee training and development, board of directors costs, depreciation, insurance expenses, facility-related costs not otherwise included in research and development expenses, professional fees for legal services, including patent-related expenses, and accounting and information technology services. As a result of the further reduction in headcount and refocusing of our development efforts announced in November 2018, we expect our general and administrative expenses to decrease in the year ending December 31, 2019 as compared to the year ended December 31, 2018.

Restructuring expenses

On January 8, 2017, we announced a reduction in headcount by approximately 30% in connection with the asset sale and the completion of our strategic pipeline review. Upon the closing of the asset sale and the completion of our strategic pipeline review, we had approximately 80 employees.

As a result of the restructuring announced on January 8, 2017 in connection with the asset sale, for the year ended December 31, 2017, we recognized total restructuring expenses of $9.5 million, which was related to contractual termination benefits for employees with pre-existing severance arrangements. These one-time employee termination benefits are comprised of severance, benefits and related costs, all of which are expected to result in cash expenditures. The majority of these payments were made during the second quarter of 2017. The remaining payments represent severance payments that were paid over one year and completed in 2018. The expense of $9.5 million was included in discontinued operations, as the costs are directly associated with the sale of the commercial business.

On November 7, 2018, we announced that we were implementing a reduction in headcount as part of a corporate restructuring, after which we expected to have approximately 27 employees. The corporate restructuring followed a comprehensive review of our drug candidate pipeline. As a result of the restructuring announced on November 7, 2018, we recognized total restructuring expenses of $1.3 million as of December 31, 2018, which was related to one-time employee termination benefits. These one-time employee termination benefits are comprised of severance, benefits and related costs, all of which are expected to result in cash expenditures. Approximately $0.4 million of these payments were made during the fourth quarter of 2018. The remaining $0.9 million will be paid over the first half of 2019.

Interest expense

Interest expense for the year ended December 31, 2018 consists primarily of cash and non-cash interest related to the Loan and Security Agreement, or loan agreement, with Hercules Capital, Inc., or Hercules, that we entered into on July 2, 2018. Interest expense for the year ended December 31, 2017 consists primarily of cash and non-cash interest related to our 4.50% convertible notes due 2020, or convertible notes, and our 11.50% senior secured notes due 2022, or 2022 notes.

In October and November 2017, we paid approximately $59.1 million, including $0.7 million for accrued and unpaid interest and $3.8 million of transaction costs, to purchase all of the remaining $60.8 million aggregate principal amount of outstanding convertible notes. We paid, in cash, an amount equal to $900 per $1,000 principal amount of convertible notes purchased, plus accrued and unpaid interest to, but not including, the date of purchase. A loss on extinguishment was recognized in interest expense in the consolidated statement of operations and comprehensive loss for year ended December 31, 2017. The $0.3 million loss on extinguishment represents the difference between the total settlement consideration transferred to the holders that was attributed to the liability component of the convertible notes, based on the fair value of that component at the time of settlement, and the net carrying value of the liability. The remaining settlement consideration transferred was allocated to the reacquisition of the embedded conversion option and recognized as a $4.2 million reduction of additional paid-in capital. Transaction costs incurred with third parties related to the conversion were allocated to the liability and equity components and resulted in an additional $3.5 million of interest expense and a $0.3 million reduction on additional paid-in capital.

In connection with the completion of the asset sale on April 3, 2017, the liability under the 2022 notes was satisfied. As a result of the early repayment of the 2022 notes, a loss on extinguishment of $25.0 million was recognized in interest expense in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2017. The $25.0 million loss on extinguishment included a $20.1 million prepayment penalty and $4.9 million of amortization expense recognized for the remaining debt discount at settlement as a result of the early repayment.

Other (expense) income, net

Other (expense) income, net consists primarily of income related to tax incentive awards, our proportionate share of earnings and losses from our equity method investment in Silver Creek, and other income or expense-related items.

Critical Accounting Policies and Significant Judgments and Estimates

Our management’s discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with the rules and regulations of the Securities and Exchange Commission, or the SEC, and generally accepted accounting principles in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenues and expenses during the reporting periods. We evaluate our estimates and judgments on an ongoing basis. Estimates included in continuing and discontinuing operations include revenue recognition, estimates utilized in the valuation of inventory, useful lives with respect to long-lived assets and intangible assets, accounting for stock-based compensation, contingencies, intangible assets, goodwill, in-process research and development, or IPR&D, tax valuation reserves and accrued expenses. We base our estimates on historical experience and on various other factors that we believe are 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. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 1, “Nature of the Business and Summary of Significant Accounting Policies,” in the accompanying notes to the consolidated financial statements appearing at the end of this Annual Report on Form 10-K, we believe that the following accounting policies are the most critical to aid in fully understanding and evaluating our financial condition and results of operations.

Accrued expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves identifying services that have been performed on our behalf and estimating the level of services performed and the associated costs incurred for such services where we have not yet been invoiced or otherwise notified of actual cost. We record these estimates in our consolidated financial statements as of each balance sheet date. Examples of estimated accrued expenses include:

- fees due to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials; and
- professional service fees.

In accruing service fees, we estimate the time period over which services will be provided and the level of effort in each period. If the actual timing of the provision of services or the level of effort varies from the estimate, we will adjust the accrual accordingly. In the event that we do not identify costs that have been incurred or we under or overestimate the level of services performed or the costs of such services, our actual expenses could differ from such estimates. The date on which some services commence, the level of services performed on or before a given date and the cost of such services are often subjective determinations. We make estimates based on the facts and circumstances known to us at the time and in accordance with GAAP. There have been no material changes in estimates for the periods presented.

Stock-based compensation expense

We account for our stock-based compensation awards in accordance with Accounting Standards Codification, or ASC, 718, Compensation – Stock Compensation. ASC 718 requires all share-based payments to employees, including grants of employee stock options, to be recognized in the consolidated statements of operations and comprehensive loss based on their grant date fair values. For stock options granted to employees and to members of our board of directors for their service on the board of directors, we estimate the grant date fair value of each option award using the Black-Scholes option pricing model. The use of the Black-Scholes option pricing model requires us to make assumptions with respect to the expected term of the option, the expected volatility of our common stock consistent with the expected term of the option, the risk-free interest rate consistent with the expected term of the option and the expected dividend yield of our common stock. Stock-based compensation expense related to employee stock options is measured using the fair value of the award at the grant date and is adjusted quarterly to reflect actual forfeitures. Stock-based compensation expense is then recognized on a straight-line basis over the vesting period, which is also the requisite service period.

We measure stock-based awards granted to non-employee consultants based on the fair value of the award on the date on which the related service is complete. Compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. At the end of each reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option pricing model.

Results of Operations

Comparison of the years ended December 31, 2018 and 2017

	Years Ended December 31,	
(in thousands)	2018	2017
Operating expenses:		
Research and development expenses	$49,974	$67,314
General and administrative expenses	15,601	28,452
Total operating expenses	65,575	95,766
Loss from continuing operations	(65,575)	(95,766)
Interest income	1,299	895
Interest expense	(956)	(34,650)
Gain on deconsolidation of Silver Creek	—	10,848
Gain on sale of asset	—	1,703
Other (expense) income, net	(3,230)	(1,433)

Net loss from continuing operations before income tax benefit	(68,462)	(118,403)
Income tax benefit	7,695	42,399
Net loss from continuing operations	$(60,767)	$(76,004)

Research and development expenses

Research and development expenses were $50.0 million for the year ended December 31, 2018 compared to $67.3 million for the year ended December 31, 2017, a decrease of $17.3 million, or 26%. This decrease was primarily attributable to:

- $21.8 million decrease in expenses related to our preclinical, general research and discovery and legacy programs related to the refocus of our early stage development spend and prioritization of our most advanced programs;
- $5.8 million decrease in stock-based compensation related to reduction in headcount; and
- $2.4 million decrease in expenses related to the timing and activity and services incurred related to the ongoing MM-310 Phase 1 clinical trial; offset by
- $12.7 million increase in expenses related to the progression of the MM-121 clinical trials and the timing of manufacturing expenses due to the nature of when runs were performed.

General and administrative expenses

General and administrative expenses were $15.6 million for the year ended December 31, 2018 compared to $28.5 million for the year ended December 31, 2017, a decrease of $12.9 million, or 45%. This decrease was primarily attributable to a decrease in corporate expenses related to reduced headcount levels and stock-based compensation in 2018 compared to 2017.

Interest income

Interest income was $1.3 million for the year ended December 31, 2018, primarily attributable to the interest income associated with our marketable securities. Interest income was $0.9 million for the year ended December 31, 2017, primarily attributable to our interest bearing cash accounts.

Interest expense

Interest expense was $1.0 million for the year ended December 31, 2018, primarily attributable to the loan agreement with Hercules. Interest expense was $34.7 million for the year ended December 31, 2017, primarily attributable to the settlement of the 2022 notes and an additional make-whole premium payment of approximately $20.1 million.

Gain on deconsolidation

We deconsolidated Silver Creek from our financial statements on July 13, 2017, the date we were no longer the primary beneficiary of Silver Creek, in accordance with ASC 810, Consolidation. As a result, we recorded a gain on the deconsolidation of Silver Creek of $10.8 million in the year ended December 31, 2017 in our consolidated statement of operations and comprehensive loss. There was no gain on deconsolidation recognized in the year ended December 31, 2018.

Other (expense) income, net

Other expense, net was $3.2 million for the year ended December 31, 2018, compared to $1.4 million for the year ended December 31, 2017. The increase was primarily attributable to our proportionate share of losses from our equity method investment in Silver Creek.

Income tax benefit (expense)

We recognized an income tax benefit of $7.7 million and $42.4 million in continuing operations for the years ended December 31, 2018 and 2017, respectively. The 2018 income tax benefit relates to the Servier milestones received, whereas the 2017 income tax benefit relates to the asset sale in 2017.

Liquidity and Capital Resources

Sources of liquidity

We have financed our operations through December 31, 2018 primarily through private placements of convertible preferred stock, collaborations, public offerings of our securities, secured debt financings, sales of ONIVYDE and the

asset sale. Through December 31, 2018, we have received $580.7 million from the asset sale, $268.2 million from the sale of convertible preferred stock and warrants, $126.7 million of net proceeds from the sale of common stock in our initial public offering and a July 2013 follow-on underwritten public offering, $38.6 million of net proceeds from our 2015 “at the market offering” program, or the ATM offering, $39.6 million of net proceeds from a secured debt financing, $120.6 million of net proceeds from the issuance of the convertible notes in our July 2013 underwritten public offering, $168.5 million of net proceeds from the issuance of the 2022 notes, $492.5 million of upfront license fees, milestone payments, reimbursement of research and development costs and manufacturing services and other payments from our collaborations, $68.9 million of cash receipts related to ONIVYDE sales, $28.0 million in milestone payments related to the development and commercialization of ONIVYDE and $14.7 million in net borrowings pursuant to the loan agreement with Hercules. As of December 31, 2018, we had unrestricted cash and cash equivalents of $ 71.3 million.

In April 2012, we closed our initial public offering pursuant to a registration statement on Form S-1, as amended. We sold an aggregate of 1,504,246 shares of common stock under the registration statement at a public offering price of $70.00 per share, including 74,246 shares pursuant to the exercise by the underwriters of an over-allotment option. Net proceeds were approximately $98.1 million, after deducting underwriting discounts and commissions and other offering expenses but prior to the payment of dividends on our Series B convertible preferred stock. At the time of our initial public offering, our convertible preferred stock and warrants to purchase convertible preferred stock automatically converted to common stock and warrants to purchase common stock, respectively.

On November 8, 2012, we entered into a loan agreement with Hercules. That loan agreement provided for an initial term loan advance of $25.0 million, which closed on November 8, 2012, and an additional term loan advance of $15.0 million, which closed on December 14, 2012 and resulted in aggregate net proceeds of $39.6 million. During the fourth quarter of 2015, we repaid the loans in full in conjunction with the issuance of the 2022 notes. We also paid an additional fee of $1.2 million that was due upon full repayment of the loans, as well as interest accrued through the repayment date.

On July 17, 2013, we sold an aggregate of 575,000 shares of our common stock at a price to the public of $50.00 per share and issued $125.0 million aggregate principal amount of convertible notes in concurrent underwritten public offerings. As a result of the concurrent common stock offering and convertible notes offering, we received aggregate net proceeds of approximately $147.3 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

On July 13, 2015, we entered into a sales agreement with Cowen and Company, LLC, or Cowen, to sell, from time to time, shares of our common stock having an aggregate sales price of up to $40.0 million through the ATM offering, under which Cowen acted as sales agent. We concluded sales under the ATM offering in September 2015, having sold approximately 0.4 million shares of common stock and generating approximately $38.6 million in net proceeds, after deducting commissions and offering expenses.

On December 22, 2015, we closed a private placement of $175.0 million aggregate principal amount of 2022 notes. As a result of the issuance of the 2022 notes, we received net proceeds of approximately $168.5 million, after deducting private placement and offering expenses payable by us.

On April 3, 2017, the liability under the 2022 notes was satisfied. As a result of the early repayment of the 2022 notes, a loss on extinguishment of $25.0 million was recognized in interest expense in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2017. The $25.0 million loss on extinguishment included a $20.1 million prepayment penalty and $4.9 million of amortization expense recognized for the remaining debt discount at settlement as a result of the early repayment.

On April 3, 2017, pursuant to the asset sale agreement with Ipsen, we retained the right to receive net milestone payments that may become payable for the ex-U.S. development and commercialization of ONIVYDE for up to $33.0 million pursuant to the Servier agreement. We entered into the Servier agreement in 2014, and on April 3, 2017, the Servier agreement was assigned to Ipsen in connection with the completion of the sale of the commercial business. To date, we have received $28.0 million of the potential $33.0 million in milestone payments under the asset sale agreement.

In October and November 2017, we paid approximately $59.1 million, including $0.7 million for accrued and unpaid interest and $3.8 million of transaction costs, to purchase all of the remaining $60.8 million aggregate principal amount of outstanding convertible notes. We paid, in cash, an amount equal to $900 per $1,000 principal amount of convertible notes purchased, plus accrued and unpaid interest to, but not including, the date of purchase. A loss on extinguishment was recognized in interest expense in the consolidated statement of operations and comprehensive loss for year ended December 31, 2017. The $0.3 million loss on extinguishment represents the difference between the total settlement consideration transferred to the holders that was attributed to the liability component of the convertible notes, based on the fair value of that component at the time of settlement, and the net carrying value of the liability. The remaining settlement consideration transferred was allocated to the reacquisition of the embedded conversion option and recognized as a $4.2 million reduction of additional paid-in capital. Transaction costs incurred with third parties related to the conversion were allocated to the liability and equity components and resulted in an additional $3.5 million of interest expense and a $0.3 million reduction on additional paid-in capital.

On July 2, 2018, we entered into the loan agreement with Hercules pursuant to which a term loan of up to an aggregate principal amount of $25.0 million is available to us. The loan agreement provides for an initial term loan advance of $15.0 million, which closed on July 2, 2018, and, at our option, two additional term loan advances of $5.0 million each upon the occurrence of certain funding conditions prior to December 31, 2018 and December 31, 2019, respectively. As a result of the decision to terminate the SHERLOC clinical trial, we do not meet the prerequisite funding conditions for drawing the two additional term loan advances under the loan agreement. We received net proceeds totaling $14.7 million.

Cash flows

The following table provides information regarding our cash flows for the years ended December 31, 2018 and 2017:

	Years Ended December 31,	
(in thousands)	2018	2017
Net cash used in operating activities	$(65,588)	$(125,811)
Net cash (used in) provided by investing activities	(22,598)	576,891
Net cash provided by (used in) financing activities	14,632	(379,163)
Net (decrease) increase in cash, cash equivalents and restricted cash	$(73,554)	$71,917

Operating activities

Cash used in operating activities was $65.6 million during the year ended December 31, 2018. The cash used in operating activities was primarily a result of our $60.8 million net loss from continuing operations and net decrease in assets and liabilities of $7.0 million. The net decrease in operating assets and liabilities during the year ended December 31, 2018 was primarily driven by the increase in prepaid expenses and other assets and decreases in accounts payable, accrued expenses and other and deferred rent and tax incentives. This decrease was offset by non-cash adjustments including $7.7 million benefit from intraperiod tax allocation, $4.1 million in depreciation and amortization, $3.1 million of stock-based compensation expense, $3.1 million in loss on equity method investment, and $0.2 million non-cash activity related to discontinued operations.

Cash used in operating activities was $125.8 million during the year ended December 31, 2017, of which $84.1 million was used by continuing operations and $41.7 million was used by discontinued operations. The cash used in operating activities was primarily a result of our $76.0 million net loss from continuing operations and net decrease in assets and liabilities of $19.6 million. The net decrease in operating assets and liabilities during the year ended December 31, 2017 was primarily driven by the increase in prepaid expenses and other assets offset by decreases in accounts payable and deferred rent. The non-cash adjustments to net loss of $11.5 million resulted in a decrease in cash used, including a $25.3 million non-cash loss on extinguishment, $17.3 million of non-cash activity related to discontinued operations, $12.8 million of stock-based compensation expense, $5.2 million of depreciation and amortization expense and $3.7 million in non-cash interest expense offset by removal of a $42.4 million income tax benefit and $10.8 million gain on deconsolidation of Silver Creek Pharmaceuticals, Inc.

Investing activities

Cash used in investing activities of $22.6 million during the year ended December 31, 2018 was primarily due to purchases of marketable securities totaling $103.1 million, offset by proceeds from maturities and sales of marketable securities totaling $52.5 million and milestone payments relating to the sale of the commercial business totaling $28.0 million.

Cash provided by investing activities of $576.9 million during the year ended December 31, 2017 was primarily due to cash received from the asset sale of $580.7 million, offset by $4.0 million of Silver Creek cash that was deconsolidated in July 2017.

Financing activities

Cash provided by financing activities of $14.6 million during the year ended December 31, 2018 was due to proceeds from the issuance of the note payable related to the loan agreement with Hercules.

Cash used in financing activities of $379.2 million during the year ended December 31, 2017 was primarily due to the $175.0 million used to settle the principle balance of the 2022 notes, $54.7 million used to settle the convertible notes, and $140.0 million dividend paid in May 2017.

Funding requirements

We have incurred significant expenses and operating losses to date, and we expect to continue to incur significant expenses and operating losses for at least the next several years. We anticipate that we would continue to incur significant expenses to the extent that we:

- continue clinical trials of our product candidates;
- continue the research and development of our other product candidates;
- seek to discover additional product candidates; and
- continue to provide the operational, financial and management information systems and personnel to support our product development.

We believe that our financial resources as of December 31, 2018 and as a result of the corporate restructuring announced on November 7, 2018, together with other restructuring and cost cutting measures that we could implement in the future, provide us with the potential to fund our operations, including debt service obligations and capital expenditure requirements, into at least the second half of 2022. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, and the extent to which we utilize collaborations with third parties to participate in their development and commercialization, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials. Our future capital requirements will depend on many factors, including:

- the progress and results of the clinical trials of our product candidates;
- our ability to establish and maintain additional collaborations on favorable terms, and the success of any such future collaborations;
- the timing and amount of potential milestone payments related to ONIVYDE that we may receive from Ipsen and Servier;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our other product candidates;
- the costs, timing and outcome of regulatory review of our current and future product candidates;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims; and
- the extent to which we acquire or invest in businesses, products and technologies.

Until such time, if ever, as we can generate sufficient product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, licensing arrangements and other marketing and distribution arrangements. We also could engage in discussions with third parties regarding partnerships, joint ventures, combinations or divestitures of one or more of our businesses as we seek to further the development of our research programs, improve our cash position and maximize stockholder value. There can be no assurance as to the timing, terms or consummation of any financing, collaboration, licensing arrangement or other marketing and distribution arrangement, partnership, joint venture, combination or divestiture. We do not have any committed external sources of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. For example, if we raise additional funds through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. 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.

Borrowings

Loan Agreement

On July 2, 2018, we entered into the loan agreement with certain subsidiaries of ours, the several banks and other financial institutions or entities from time to time parties thereto, which we collectively refer to as Lender, and Hercules, in its capacity as administrative agent and collateral agent for itself and Lender, which we refer to in such capacity as Agent, pursuant to which a term loan of up to an aggregate principal amount of $25.0 million is available

to us. The loan agreement provides for an initial term loan advance of $15.0 million, which closed on July 2, 2018, and, at our option, two additional term loan advances of $5.0 million each upon the occurrence of certain funding conditions prior to December 31, 2018 and December 31, 2019, respectively. As a result of our decision to terminate the SHERLOC clinical trial in October 2018, we do not meet the prerequisite funding conditions for drawing the two additional term loan advances.

The term loan bears interest at an annual rate equal to the greater of 9.25% and 9.25% plus the prime rate of interest minus 5.25%. The loan agreement provides for interest-only payments for eighteen months and repayment of the aggregate outstanding principal balance of the term loan in monthly installments starting on February 1, 2020 and continuing through August 1, 2021, or the loan maturity date. In addition, we paid a fee of $0.3 million upon closing and are required to pay a fee of 5.55% of the aggregate amount of advances under the loan agreement at maturity. At our option, we may elect to prepay all, but not less than all, of the outstanding term loan by paying the entire principal balance and all accrued and unpaid interest thereon plus a prepayment charge equal to the following percentage of the principal amount being prepaid: 3% if the term loan is prepaid during the first 12 months following the initial closing and 1% if the term loan is prepaid any time thereafter but prior to the loan maturity date.

In connection with the loan agreement, we granted Agent a security interest in all of our personal property now owned or hereafter acquired, excluding intellectual property but including licenses of and the proceeds from the sale, if any, of intellectual property, and a negative pledge on intellectual property. The loan agreement also contains certain events of default, representations, warranties and non-financial covenants of us. In addition, the loan agreement grants Lender an option to purchase up to an aggregate of $1.0 million of the our equity securities, or instruments exercisable for or convertible into equity securities, sold to investors in any private financing within one year after the initial closing under the loan agreement upon the same terms and conditions afforded to such other investors.

11.50% senior secured notes due 2022

In December 2015, we closed a private placement of $175.0 million aggregate principal amount of 2022 notes and entered into an indenture with U.S. Bank National Association as trustee and collateral agent. As a result of this placement, we received net proceeds of approximately $168.5 million, after deducting private placement and offering expenses payable by us.

In connection with the completion of the asset sale, on April 3, 2017, we irrevocably deposited the aggregate redemption price of the 2022 notes of 111.5% of the principal amount, plus accrued and unpaid interest of $7.4 million, with the trustee and irrevocably instructed the trustee to apply such amount to the redemption in full of the 2022 notes on the redemption date of April 27, 2017. The indenture was satisfied and discharged on April 3, 2017.

4.50% convertible notes due 2020

In July 2013, we issued $125.0 million aggregate principal amount of convertible notes. We issued the convertible notes under a base indenture between us and Wells Fargo Bank, National Association, as trustee, as supplemented by a supplemental indenture between us and the trustee. As a result of the convertible notes offering, we received net proceeds of approximately $120.6 million, after deducting underwriting discounts and commissions and offering expenses payable by us.

The convertible notes bear interest at a rate of 4.50% per year, payable semiannually in arrears on January 15 and July 15 of each year, beginning on January 15, 2014. The convertible notes are general unsecured senior obligations of ours and rank (i) pari passu in seniority with respect to the 2022 notes, (ii) senior in right of payment to any of our indebtedness that is expressly subordinated in right of payment to the convertible notes, (iii) equal in right of payment to any of our unsecured indebtedness that is not so subordinated, (iv) effectively junior in right of payment to any of our secured indebtedness to the extent of the value of the assets securing such indebtedness, and (v) structurally junior to all indebtedness and other liabilities (including trade payables) of our subsidiaries.

On April 13, 2016, we entered into separate, privately-negotiated conversion agreements with certain holders of the convertible notes. Under the conversion agreements, such holders agreed to convert an aggregate principal amount of $64.2 million of convertible notes held by them. We initially settled each $1,000 principal amount of convertible notes surrendered for conversion by delivering 14 shares of our common stock on April 18, 2016. In total, we issued an aggregate of 873,215 shares of our common stock on this initial closing date. In addition, pursuant to the conversion agreements, at the additional closings (as defined in the conversion agreements), we issued an aggregate of 363,511 shares of our common stock representing an aggregate of $27.7 million as additional payments in respect of the conversion of the convertible notes. The number of additional shares was determined based on the daily VWAP (as defined in the conversion agreements) of our common stock for each of the trading days in the 10-day trading period following the date of the conversion agreements.

The outstanding convertible notes will mature on July 15, 2020, or the maturity date, unless earlier repurchased by us or converted at the option of holders. Holders may convert their convertible notes at their option at any time prior to

the close of business on the business day immediately preceding April 15, 2020 only under the following circumstances:

- during any calendar quarter commencing after September 30, 2013 (and only during such calendar quarter), if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;
- during the five business day period after any five consecutive trading day period, or the measurement period, in which the trading price (as defined in the convertible senior notes) per $1,000 principal amount of convertible senior notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our common stock and the conversion rate on each such trading day; or
- upon the occurrence of specified corporate events set forth in the indenture.

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On or after April 15, 2020 until the close of business on the business day immediately preceding the maturity date, holders may convert their convertible notes at any time, regardless of the foregoing circumstances.

The convertible notes may be settled, at our election, in cash, shares of our common stock or a combination of cash and shares of our common stock.

The initial conversion rate of the convertible notes upon issuance in July 2013 was 160.0000 shares of our common stock per $1,000 principal amount of convertible notes, which was equivalent to an initial conversion price of $6.25 per share of common stock. As a result of the special cash dividend that was payable on May 26, 2017 to stockholders of record as of the close of business on May 17, 2017, the conversion rate of the convertible notes was adjusted from 160.0000 shares of our common stock per $1,000 principal amount of convertible notes to 235.2112 shares of our common stock per $1,000 principal amount of convertible notes. As a result of the one-for-ten reverse stock split of our common stock effected on September 5, 2017, the conversion rate of the convertible notes was further adjusted from 235.2112 shares of our common stock per $1,000 principal amount of convertible notes to 23.5210 shares of our common stock per $1,000 principal amount of convertible notes. The conversion rate will be subject to further adjustment in some events, but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date, we will increase the conversion rate for a holder who elects to convert its convertible notes in connection with such a corporate event in certain circumstances.

Upon the occurrence of a fundamental change (as defined in the indenture) involving us, holders of the convertible notes may require us to repurchase all or a portion of their convertible notes for cash at a price equal to 100% of the principal amount of the convertible notes to be purchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date.

The indenture contains customary terms and covenants and events of default with respect to the convertible notes. If an event of default (as defined in the indenture) occurs and is continuing, the trustee by written notice to us, or the holders of at least 25% in aggregate principal amount of the convertible notes then outstanding by written notice to us and the trustee, may, and the trustee at the request of such holders will, declare 100% of the principal of and accrued and unpaid interest on the convertible notes to be due and payable. In the case of an event of default arising out of certain events of bankruptcy, insolvency or reorganization involving us or a significant subsidiary (as set forth in the indenture), 100% of the principal of and accrued and unpaid interest on the convertible notes will automatically become due and payable.

In October and November 2017, we paid approximately $59.1 million, including $0.7 million for accrued and unpaid interest and $3.8 million of transaction costs, to purchase all of the remaining $60.8 million aggregate principal amount of outstanding convertible notes. We paid, in cash, an amount equal to $900 per $1,000 principal amount of convertible notes purchased, plus accrued and unpaid interest to, but not including, the date of purchase. A loss on extinguishment was recognized in interest expense in the consolidated statement of operations and comprehensive loss for year ended December 31, 2017. The $0.3 million loss on extinguishment represents the difference between the total settlement consideration transferred to the holders that was attributed to the liability component of the convertible notes, based on the fair value of that component at the time of settlement, and the net carrying value of the liability. The remaining settlement consideration transferred was allocated to the reacquisition of the embedded conversion option and recognized as a $4.2 million reduction of additional paid-in capital. Transaction costs incurred with third parties related to the conversion were allocated to the liability and equity components and resulted in an additional $3.5 million of interest expense and a $0.3 million reduction on additional paid-in capital.

Certain Contractual Obligations and Commitments

Expenditures to contract research organizations represent a significant cost in clinical development. However, our contracts with these research organizations are cancellable at our option upon short notice and do not have cancellation penalties.

On July 2, 2018, we entered into the loan agreement, as amended, with Hercules pursuant to which a term loan of up to an aggregate principal amount of $25.0 million is available to us. The loan agreement provides for an initial term loan advance of $15.0 million, which closed on July 2, 2018, and, at our option, two additional term loan advances of $5.0 million each upon the occurrence of certain funding conditions prior to December 31, 2018 and December 31, 2019, respectively. As a result of the decision to terminate the SHERLOC clinical trial, we do not meet the prerequisite funding conditions for drawing the two additional term loan advances under the loan agreement. The term loan bears interest at an annual rate equal to the greater of 9.25% and 9.25% plus the prime rate of interest minus 5.25%. The loan agreement provides for interest-only payments for eighteen months and repayment of the aggregate outstanding principal balance of the term loan in monthly installments starting on February 1, 2020 and continuing through August 1, 2021. In addition, we paid a fee of $0.3 million upon closing and are required to pay a fee of 5.55% of the aggregate amount of advances under the loan agreement at maturity.

In May 2014, the Massachusetts Life Sciences Center, or the MLSC, awarded us an additional $0.6 million of tax incentives under its Life Science Tax Incentive Program, which allows us to monetize approximately $0.6 million of state research and development tax credits. In exchange for these incentives, we pledged to hire an incremental 31 employees and to maintain the additional headcount through at least December 31, 2018. Due to our failure to meet this headcount target as of December 31, 2016 as a result of our October 2016 corporate restructuring activities, we will be required to repay approximately $0.3 million of this award.

In March 2015, the MLSC awarded us an additional $1.4 million of tax incentives under its Life Science Tax Incentive Program, which allows us to monetize approximately $1.2 million of state research and development tax credits. In exchange for these incentives, we pledged to hire an incremental 75 employees and to maintain the additional headcount through at least December 31, 2019. Due to our failure to meet this headcount target as of December 31, 2016 as a result of our October 2016 corporate restructuring activities, we will be required to repay approximately $1.0 million of this award.

Off-Balance Sheet Arrangements

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

Tax Loss Carryforwards

At December 31, 2018, we had net operating loss carryforwards for federal and state income tax purposes of $179.7 million and $263.9 million, respectively. Our existing federal and state net operating loss carryforwards begin to expire in 2031. We also had available research and development credits for federal and state income tax purposes of approximately $28.8 million and $18.9 million, respectively. The federal and state research and development credits will begin to expire in 2022 and 2025, respectively. As of December 31, 2018, we also had available investment tax credits for state income tax purposes of $0.1 million, which began to expire in 2019. We have Orphan Drug Credits of $122.5 million, which begin to expire in 2031.

We have evaluated the positive and negative evidence bearing upon the realizability of our deferred tax assets, which are comprised principally of net operating loss carryforwards and research and development credits. Under the applicable accounting standards, we have considered our history of losses and concluded that it is more likely than not that we will not recognize the benefits of federal and state deferred tax assets. Accordingly, a full valuation allowance has been established against the deferred tax assets. In the second quarter of 2017, when the asset sale was consummated, we utilized deferred tax assets. The valuation allowance was released during the year ended December 31, 2017 when we determined it is more likely than not that the deferred tax assets will be realizable in that period.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Tax Cuts and Jobs Act, or the TCJA. We have recognized the provisional tax impacts related to the revaluation of the deferred tax assets and liabilities and included these amounts in our consolidated financial statements for the year ended December 31, 2018.

Utilization of the net operating loss and tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, or the Internal Revenue Code, due to ownership change limitations that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and tax credit carryforwards that can be utilized annually to offset future taxable income and tax. We completed an evaluation of ownership changes through December 31, 2017 to assess whether

utilization of our net operating loss or tax credit carryforwards would be subject to an annual limitation under Section 382 of the Internal Revenue Code. We believe that we can utilize all of our existing tax attributes as a result of the analysis. To the extent an ownership change occurs in the future, the net operating loss and tax credit carryforwards may be subject to limitation.

We have not, as of yet, conducted a study of our domestic research and development credit carryforwards and Orphan Drug Credits. This study may result in an increase or decrease to our credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against our credits, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. As a result, there would be no impact to the statement of operations and comprehensive loss, balance sheet or cash flows if an adjustment were required.

Recent Accounting Pronouncements

See Note 1, “Nature of the Business and Summary of Significant Accounting Policies,” in the accompanying notes to the consolidated financial statements for a description of recent accounting pronouncements applicable to our business.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We invest in a variety of financial instruments, principally cash deposits, money market funds, securities issued by the U.S. government and its agencies and corporate debt securities. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and fiduciary control of cash and investments. We also seek to maximize income from our investments without assuming significant risk.

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of interest rates, particularly because our investments are in short-term marketable securities. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our portfolio. We have the ability and intention to hold our investments until maturity, and therefore, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a sudden change in market interest rates on our investment portfolio.

We do not currently have any auction rate or mortgage-backed securities. We do not believe our cash, cash equivalents and marketable securities have significant risk of default or illiquidity, however we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-30 of this Annual Report on Form 10-K.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2018. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that

any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2018, our Chief Executive Officer and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Internal Control Over Financial Reporting

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for the company. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's 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 GAAP and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2018. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013). Based on its assessment, management concluded that, as of December 31, 2018, our internal control over financial reporting is effective based on those criteria.

The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report, which appears herein.

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 three months 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 10 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC with respect to our 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(1) Financial Statements
Our consolidated financial statements are set forth on pages F-1 through F-30 of this Annual Report on Form 10-K and are incorporated herein by reference.

(2) Financial Statement Schedules
Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(3) Exhibits

Exhibit Number	Description of Exhibit
1.1	Sales Agreement, dated as of December 15, 2017, by and between the Registrant and Cowen and Company, LLC (incorporated by reference to Exhibit 1.2 to the Registrant's Registration Statement on Form S-3 filed on December 15, 2017)
2.1	Asset Purchase and Sale Agreement, dated as of January 7, 2017, by and between the Registrant and Ipsen S.A. (incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K filed on January 9, 2017)
3.1	Restated Certificate of Incorporation of the Registrant, as amended (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q filed on August 7, 2018)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.5 to the Registrant's Registration Statement on Form S-1, as amended, filed on January 13, 2012)
4.1	Specimen certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.1 to the Registrant's Annual Report on Form 10-K filed on March 12, 2018)
4.2	Indenture, dated as of July 17, 2013, by and between the Registrant and Wells Fargo Bank, National Association, as trustee (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed on July 18, 2013)
4.3	First Supplemental Indenture, dated as of July 17, 2013, by and between the Registrant and Wells Fargo Bank, National Association, as trustee (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K filed on July 18, 2013)
10.1#	2008 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1, as amended, filed on July 8, 2011)
10.2#	2011 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1, as amended, filed on January 13, 2012)

10.3#	Form of Incentive Stock Option Agreement under 2011 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1, as amended, filed on January 13, 2012)
10.4#	Form of Non-Qualified Stock Option Agreement under 2011 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1, as amended, filed on January 13, 2012)
10.5#	Employment Agreement, dated as of January 17, 2017, by and between the Registrant and Richard Peters (incorporated by reference to Exhibit 10.6 to the Registrant's Annual Report on Form 10-K filed on March 1, 2017)
10.6#	Employment Agreement, dated as of May 4, 2017, by and between the Registrant and Sergio L. Santillana (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2017)
10.7#	Employment Agreement, dated as of May 1, 2017, by and between the Registrant and Daryl C. Drummond (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2017)
10.8#	Employment Agreement, dated as of February 24, 2015, by and between the Registrant and Jeffrey A. Munsie (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2017)

Exhibit Number	Description of Exhibit
10.9#	Employment Agreement, dated as of August 10, 2017, by and between the Registrant and Jean M. Franchi (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed on November 8, 2017)
10.10#	Retention Bonus Agreement, dated as of April 3, 2017, by and between the Registrant and Jeffrey A. Munsie (incorporated by reference to Exhibit 10.7 to the Registrant's Quarterly Report on Form 10-Q filed on May 10, 2017)
10.11#	Scientific Advisory Board Consulting and Confidentiality Agreement, dated as of February 6, 2018, by and between the Registrant and George D. Demetri (incorporated by reference to Exhibit 10.11 to the Registrant's Annual Report on Form 10-K filed on March 12, 2018)
10.12#	Form of Indemnification Agreement between the Registrant and each director and executive officer (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1, as amended, filed on August 19, 2011)
10.13	Indenture of Lease, dated as of August 24, 2012, by and between the Registrant and DWF IV One Kendall, LLC (as successor-in-interest to RB Kendall Fee, LLC), as amended by the First Amendment of Lease, dated as of March 18, 2013 (incorporated by reference to Exhibit 10.14 to the Registrant's Annual Report on Form 10-K filed on March 20, 2013)
10.14	Second Amendment of Lease, dated as of September 12, 2013, by and between the Registrant and DWF IV One Kendall, LLC (as successor-in-interest to RB Kendall Fee, LLC) (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed on November 8, 2013)
10.15	Third Amendment of Lease, dated as of February 23, 2015, by and between the Registrant and DWF IV One Kendall, LLC (incorporated by reference to Exhibit 10.15 to the Registrant's Annual Report on Form 10-K filed on February 27, 2015)
10.16	Fourth Amendment of Lease, dated as of July 22, 2015, by and between the Registrant and DWF IV One Kendall, LLC (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed on November 9, 2015)
10.17	Fifth Amendment of Lease, dated as of April 3, 2017, by and between the Registrant and ARE-MA Region No. 59, LLC (incorporated by reference to Exhibit 10.8 to the Registrant's Quarterly Report on Form 10-Q filed on May 10, 2017)
10.18	Sixth Amendment of Lease, dated as of June 9, 2017, by and between the Registrant and ARE-MA Region No. 59, LLC (incorporated by reference to Exhibit 10.11 to the Registrant's Quarterly Report on Form 10-Q filed on August 9, 2017)
10.19	Seventh Amendment of Lease, dated as of February 6, 2018, by and between the Registrant and ARE-MA Region No. 59, LLC (incorporated by reference to Exhibit 10.23 to the Registrant's Annual Report on Form 10-K filed on March 12, 2018)

10.20	Eighth Amendment of Lease, dated as of February 15, 2018, by and between the Registrant and ARE-MA Region No. 59, LLC (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed on May 8, 2018)
10.21	Sublease Agreement, dated as of April 3, 2017, by and between the Registrant and Ipsen Bioscience, Inc. (incorporated by reference to Exhibit 10.9 to the Registrant's Quarterly Report on Form 10-Q filed on May 10, 2017)
10.22†	Exclusive License Agreement, dated as of November 1, 2000, by and between the Registrant (as successor-in-interest to Hermes BioSciences, Inc.) and The Regents of the University of California, as amended on October 6, 2003, September 13, 2006, June 6, 2007 and September 28, 2007 (incorporated by reference to Exhibit 10.20 to the Registrant's Registration Statement on Form S-1, as amended, filed on October 26, 2011)
10.23†	Collaboration Agreement, dated as of November 16, 2009, by and between the Registrant and Adimab LLC, as amended on April 27, 2010, June 2, 2010 and October 11, 2011 (incorporated by reference to Exhibit 10.22 to the Registrant's Registration Statement on Form S-1, as amended, filed on October 26, 2011)
10.24†	Sublicense Agreement, dated as of June 30, 2008, by and between the Registrant and Dyax Corp. (incorporated by reference to Exhibit 10.23 to the Registrant's Registration Statement on Form S-1, as amended, filed on July 8, 2011)
10.25†	Amended and Restated Collaboration Agreement, dated as of January 24, 2007, by and between the Registrant and Dyax Corp., as amended on July 31, 2008 and November 6, 2009 (incorporated by reference to Exhibit 10.24 to the Registrant's Registration Statement on Form S-1, as amended, filed on October 26, 2011)
10.26	Amendment to Amended and Restated Collaboration Agreement, dated as of January 18, 2012, by and between the Registrant and Dyax Corp. (incorporated by reference to Exhibit 10.26 to the Registrant's Annual Report on Form 10-K filed on March 20, 2013)

Exhibit Number	Description of Exhibit
10.27	Loan and Security Agreement, dated as of July 2, 2018, by and among the Registrant, certain subsidiaries of the Registrant from time to time party thereto, the several banks and other financial institutions or entities from time to time parties thereto and Hercules Capital, Inc. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on July 3, 2018)
10.28*	Consent and Amendment No. 1 to Loan and Security Agreement, dated as of December 27, 2018, by and among the Registrant, the several banks and other financial institutions or entities from time to time parties thereto and Hercules Capital, Inc.
10.29	Stipulation and Agreement of Settlement and Release, dated as of October 6, 2017, by and among the Registrant, Wells Fargo Bank, National Association, Wolverine Flagship Fund Trading Limited, 1992 MSF International Ltd (formerly known as Highbridge International LLC) and 1992 Tactical Credit Master Fund, L.P. (formerly known as Highbridge Tactical Credit & Convertibles Master Fund, L.P.) (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed on October 10, 2017)
21.1*	Subsidiaries of the Registrant
23.1*	Consent of PricewaterhouseCoopers LLP, an independent registered public accounting firm
31.1*	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1+	Certification of Principal 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 Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Database
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

*Filed herewith.
+Furnished herewith.
#Management contract or compensatory plan, contract or agreement.
†Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

MERRIMACK PHARMACEUTICALS, INC.

Date: March 6, 2019 By: /s/ Richard Peters, M.D., Ph.D.
Richard Peters, M.D., Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Richard Peters, M.D., Ph.D. Richard Peters, M.D., Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 6, 2019
/s/ Jean M. Franchi Jean M. Franchi	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	March 6, 2019
/s/ Gary L. Crocker Gary L. Crocker	Chairman of the Board	March 6, 2019
/s/ George D. Demetri, M.D. George D. Demetri, M.D.	Director	March 6, 2019
/s/ John M. Dineen John M. Dineen	Director	March 6, 2019
/s/ Ulrik B. Nielsen, Ph.D. Ulrik B. Nielsen, Ph.D.	Director	March 6, 2019
/s/ James H. Quigley James H. Quigley	Director	March 6, 2019
/s/ Russell T. Ray Russell T. Ray	Director	March 6, 2019

MERRIMACK PHARMACEUTICALS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Merrimack Pharmaceuticals, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Merrimack Pharmaceuticals, Inc. and its subsidiaries (the “Company”) as of December 31, 2018 and 2017, and the related consolidated statements of operations and comprehensive loss, of non-controlling interest and stockholders’ equity (deficit) and of cash flows for the years then ended, including the related notes (collectively referred to as the “consolidated financial statements”). We also have audited the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control - Integrated Framework (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management’s Annual Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company’s consolidated financial statements and on the Company's internal control over financial reporting 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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements 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. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

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

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Emphasis of Matter

As discussed in Note 1 to the consolidated financial statements, the Company will require additional financing to fund future operations. Management's evaluation of the events and conditions and management's plans to mitigate this matter are also described in Note 1.

/s/PricewaterhouseCoopers LLP

Boston, Massachusetts

March 6, 2019

We have served as the Company's auditor since 2002.

Merrimack Pharmaceuticals, Inc.

Consolidated Balance Sheets

(in thousands, except per share amounts)	December 31, 2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$20,079	$93,441
Marketable securities	51,199	—
Restricted cash	584	102
Accounts receivable, net	—	100
Prepaid expenses and other current assets	4,240	1,403
Total current assets	76,102	95,046
Restricted cash	—	674
Property and equipment, net	2,269	6,467
Equity method investment	7,428	10,551
Other assets	2,744	4,588
Total assets	$88,543	$117,326
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable, accrued expenses and other	$13,677	$17,606
Deferred rent	1,118	2,171
Total current liabilities	14,795	19,777
Deferred rent, net of current portion	—	1,209
Note payable, net of discount	14,873	—
Other long-term liabilities	56	56
Total liabilities	29,724	21,042
Commitments and contingencies (Note 15)		
Stockholders' equity:		
Preferred stock, $0.01 par value: 10,000 shares authorized at December 31, 2018 and 2017; no shares issued or outstanding at December 31, 2018 or 2017	—	—
Common stock, $0.01 par value: 30,000 and 20,000 shares authorized at December 31, 2018 and 2017, respectively; 13,343 issued and outstanding at December 31, 2018 and 2017	1,334	1,334
Additional paid-in capital	580,771	577,721
Accumulated other comprehensive loss	(9)	—
Accumulated deficit	(523,277)	(482,771)
Total stockholders' equity	58,819	96,284
Total liabilities and stockholders' equity	$88,543	$117,326

The accompanying notes are an integral part of these consolidated financial statements.

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Merrimack Pharmaceuticals, Inc.

Consolidated Statements of Operations and Comprehensive Loss

(in thousands, except per share amounts)	Years Ended December 31, 2018	2017
Operating expenses:		
Research and development expenses	$49,974	$67,314
General and administrative expenses	15,601	28,452
Total operating expenses	65,575	95,766
Loss from continuing operations	(65,575)	(95,766)
Other income and expenses:		
Interest income	1,299	895
Interest expense	(956)	(34,650)
Gain on deconsolidation of Silver Creek Pharmaceuticals, Inc.	—	10,848
Gain on sale of asset	—	1,703
Other (expense) income, net	(3,230)	(1,433)
Total other income and expenses	(2,887)	(22,637)
Net loss from continuing operations before income tax benefit	(68,462)	(118,403)
Income tax benefit	7,695	42,399
Net loss from continuing operations	(60,767)	(76,004)
Discontinued operations:		
Income from discontinued operations, net of tax	20,261	546,872
Net (loss) income	(40,506)	470,868
Net loss attributable to non-controlling interest	—	(1,160)
Net (loss) income attributable to Merrimack Pharmaceuticals, Inc.	$(40,506)	$472,028
Other comprehensive loss:		
Unrealized loss on marketable securities	(9)	—
Other comprehensive loss	(9)	—
Comprehensive (loss) income	$(40,515)	$472,028
Amounts attributable to Merrimack Pharmaceuticals, Inc.:		
Net loss from continuing operations	$(60,767)	$(74,844)
Income from discontinued operations, net of tax	20,261	546,872
Net (loss) income attributable to Merrimack Pharmaceuticals, Inc.	$(40,506)	$472,028
Basic and dilutive net (loss) income per common share		
Net loss from continuing operations	$(4.55)	$(5.66)
Net income from discontinued operations, net of tax	$1.52	41.33
Net (loss) income per share	$(3.03)	$35.67
Weighted-average common shares used in per share calculations—basic and diluted	13,343	13,232

The accompanying notes are an integral part of these consolidated financial statements.

Merrimack Pharmaceuticals, Inc.

Consolidated Statements of Non-Controlling Interest

and Stockholders' Equity (Deficit)

		Common Stock			Accumulated		Total
(in thousands)	Non-Controlling Interest	Shares	Amount	Additional Paid-In Capital	Other Comprehensive Loss	Accumulated Deficit	Stockholders' Equity (Deficit)
Balance at December 31, 2016	$ (1,539)	13,020	$ 1,302	$ 702,377	$ —	$ (954,799)	$ (251,120)
Exercise of stock options	—	323	32	6,657	—	—	6,689
Consideration allocated to reacquisition of conversion feature on extinguishment of convertible notes due 2020	—	—	—	(4,481)	—	—	(4,481)
Dividend paid	—	—	—	(140,000)	—	—	(140,000)
Issuance of Series C preferred stock by Silver Creek Pharmaceuticals, Inc.	847	—	—	—	—	—	—
Stock-based compensation	—	—	—	13,168	—	—	13,168
Loss attributable to non-controlling interest	(1,160)	—	—	—	—	1,160	1,160
Deconsolidation of non-controlling interest	1,852	—	—	—	—	—	—
Net income	—	—	—	—	—	470,868	470,868
Balance at December 31, 2017	$ —	13,343	$ 1,334	$ 577,721	$ —	$ (482,771)	$ 96,284
Stock-based compensation	—	—	—	3,050	—	—	3,050
Unrealized loss on marketable securities	—	—	—	—	(9)	—	(9)
Net loss	—	—	—	—	—	(40,506)	(40,506)
Balance at December 31, 2018	$ —	13,343	$ 1,334	$ 580,771	$ (9)	$ (523,277)	$ 58,819

The accompanying notes are an integral part of these consolidated financial statements.

Merrimack Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows

(in thousands)	Years Ended December 31, 2018	2017
Cash flows from operating activities		
Net (loss) income	$(40,506)	$470,868
Less:		
Income from discontinued operations	20,261	546,872
Loss from continuing operations	(60,767)	(76,004)
Adjustments to reconcile net loss to net cash used in operating activities		
Non-cash interest expense	240	3,678
Purchased premiums and interest on marketable securities	(2)	—
Amortization and accretion on marketable securities	(651)	—
Loss on extinguishment of debt	—	25,326
Non-cash activity related to discontinued operations	(171)	17,282
Benefit from intra period tax allocation	(7,695)	(42,399)
Loss on disposal of property and equipment	167	—
Gain on sale of property and equipment	—	(439)
Depreciation and amortization expense	4,074	5,221
Stock-based compensation expense	3,050	12,788
Loss on equity method investment	3,123	849
Gain on deconsolidation of Silver Creek Pharmaceuticals, Inc.	—	(10,848)
Changes in operating assets and liabilities:		
Accounts receivable	100	175
Prepaid expenses and other assets	(993)	(8,476)
Accounts payable, accrued expenses and other	(3,801)	(9,278)
Deferred rent	(2,262)	(2,021)
Net cash used in continuing operations for operating activities	(65,588)	(84,146)
Net cash used in discontinued operations for operating activities	—	(41,665)
Net cash used in operating activities	(65,588)	(125,811)
Cash flows from investing activities		
Purchase of marketable securities	(103,055)	—
Proceeds from sales and maturities of marketable securities	52,500	—
Purchase of property and equipment	(118)	(915)
Deconsolidation of Silver Creek Pharmaceuticals, Inc.	—	(4,002)
Proceeds on sale of property and equipment	75	1,094
Proceeds from sale of a discontinued operation	28,000	580,714
Net cash (used in) provided by continuing operations for investing activities	(22,598)	576,891
Cash flows from financing activities		
Payment of debt extinguishment costs	—	(20,124)
Proceeds from exercise of options and warrants to purchase common stock	—	6,917
Proceeds from issuance of note payable, net of issuance costs	14,632	—
Proceeds from issuance of preferred stock by Silver Creek Pharmaceuticals, Inc.	—	3,994
Repayment of debt	—	(229,662)

Payment of dividend	—	(140,000)
Other financing activities, net	—	(288)
Net cash provided by (used in) financing activities	14,632	(379,163)
Net (decrease) increase in cash, cash equivalents and restricted cash	(73,554)	71,917
Cash, cash equivalents and restricted cash, beginning of period	94,217	22,300
Cash, cash equivalents and restricted cash, end of period	$20,663	$94,217
Non-cash investing and financing activities		
Purchases of property and equipment in accounts payable, accrued expenses and other	$—	$14
Supplemental disclosure of cash flows		
Cash paid for income taxes	$390	$7,926
Cash paid for interest	586	30,966

The accompanying notes are an integral part of these consolidated financial statements.

Merrimack Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

1. Nature of the Business and Summary of Significant Accounting Policies

Nature of the Business

Merrimack Pharmaceuticals, Inc. (the "Company") is a clinical stage biopharmaceutical company based in Cambridge, Massachusetts that is outthinking cancer by targeting biomarker-defined cancers. The Company's vision is to ensure that cancer patients and their families live fulfilling lives. The Company's mission is to transform cancer care through the smart design and development of targeted solutions based on a deep understanding of cancer pathways and biological markers. The Company's strategy is to (1) understand the biological problems it is trying to solve, (2) design specific solutions against the problems it is trying to solve and (3) develop those solutions for biomarker-selected patients. This three-pronged strategy seeks to ensure optimal patient outcomes. The Company owns worldwide development and commercial rights to all of its clinical and preclinical programs.

On April 3, 2017, the Company completed the asset sale (the "Asset Sale") with Ipsen S.A. ("Ipsen"). Pursuant to the Asset Purchase and Sale Agreement, dated as of January 7, 2017 (the "Asset Sale Agreement"), between the Company and Ipsen, the Company sold to Ipsen its right, title and interest in the non-cash assets, equipment, inventory, contracts and intellectual property primarily related to or used in the Company's business operations and activities involving or relating to developing, manufacturing and commercializing ONIVYDE and MM-436 (the "Commercial Business"). The Company received $575.0 million in cash, plus a working capital adjustment of $5.7 million, and is eligible to receive up to $450.0 million in additional regulatory approval-based milestone payments. The working capital adjustment of $5.7 million was agreed to with Ipsen and received by the Company in the year ended December 31, 2017. The Company also retained the right to receive net milestone payments that may become payable for the ex-U.S. development and commercialization of ONIVYDE for up to $33.0 million pursuant to a license and collaboration agreement (the "Servier Agreement") between Ipsen S.A. ("Ipsen") and Les Laboratoires Servier SAS ("Servier") (as assignee from Shire plc). The Company entered into the Servier Agreement in 2014, and on April 3, 2017, the Servier Agreement was assigned to Ipsen in connection with the completion of the Asset Sale. The Company's non-commercial assets, including its clinical and preclinical development programs, were not included in the Asset Sale and remain assets of the Company.

The Company's only clinical stage asset in active development is MM-310. MM-310 is an antibody-directed nanotherapeutic that targets the ephrin receptor A2 ("EphA2") receptor and contains a novel cytotoxic taxane. The EphA2 receptor is highly expressed in most solid tumor types, such as prostate, ovarian, bladder, gastric, pancreatic and lung cancers. The Company is conducting a Phase 1 clinical trial to evaluate safety and preliminary activity of MM-310 in patients with solid tumors and to identify the maximum tolerated dose.

The Company's two most promising preclinical programs are MM-401, an agonistic antibody targeting a novel immuno-oncology target, TNFR2, and MM-201, a highly stabilized agonist-Fc fusion protein targeting death receptors 4 and 5.

The Company is subject to risks and uncertainties common to companies in the biopharmaceutical industry, including, among other things, its ability to secure additional capital to fund operations, success of clinical trials, development by competitors of new technological innovations, dependence on collaborative arrangements, protection of proprietary technology, compliance with government regulations and dependence on key personnel. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant

amounts of capital, adequate personnel, infrastructure and extensive compliance reporting capabilities.

The Company's product candidates are in development. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary government regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies, among others. In addition, the Company is dependent upon the services of its employees and consultants.

In accordance with Accounting Standards Codification ("ASC") 205-40, Going Concern, the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. As of December 31, 2018, the Company had an accumulated deficit of $523.3 million. During the year ended December 31, 2018, the Company incurred a net loss from continuing operations of $60.8 million and used $65.6 million of cash in continuing operations for operating activities. The Company expects to continue to generate operating losses in the foreseeable future. The Company expects that its cash, cash equivalents and marketable securities of $71.3 million at December 31, 2018 will be sufficient to fund its operating expenses and capital expenditure requirements for at least the next 12 months from issuance of the financial statements. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations.

The Company will ultimately need to seek additional funding through public or private equity or debt financings, through existing or new collaboration arrangements, or through divestitures of its assets. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into additional collaborative arrangements or divest its assets. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. Arrangements with collaborators or others may require the Company to relinquish rights to certain of its technologies or product candidates. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate its research and development programs or commercialization efforts, which could adversely affect its business prospects.

Summary of Significant Accounting Policies

Segment Information

Operating segments are defined as components of an enterprise engaging in business activities for which discrete financial information is available and regularly reviewed by the chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business as one operating segment and the Company operates in only one geographic region (the United States).

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared under U.S. generally accepted accounting principles ("GAAP") and include the accounts of the Company and its wholly owned subsidiaries.

As of March 31, 2017, the Commercial Business met all the conditions to be classified as held-for-sale and represents a discontinued operation since the disposal of the Commercial Business is a strategic shift that will have a major effect on the Company's operations and financial results. The Company will not have further significant involvement in the operations of the discontinued Commercial Business. The operating results of the Commercial Business are reported as discontinued operations, net of tax in the consolidated statements of operations and comprehensive loss for all periods presented. For additional information, see Note 2, "Discontinued Operations – Sale of Commercial Business."

The consolidated financial statements have historically included the accounts of the Company and Silver Creek Pharmaceuticals, Inc. ("Silver Creek") with all intercompany transactions and balances eliminated in consolidation. Silver Creek represented a variable interest entity that the Company consolidated as the primary beneficiary. As discussed in Note 3, "Investment in Silver Creek," Silver Creek completed a preferred stock financing in the third quarter of 2017, which reduced the Company's ownership percentage in Silver Creek below 50% and resulted in the Company no longer controlling the Silver Creek board of directors. The Company determined that it is no longer the primary beneficiary of Silver Creek since the Company does not control the board of directors and does not direct the activities that have the most significant impact on Silver Creek's economic performance. Therefore, the Company

deconsolidated Silver Creek from its financial statements in the third quarter of 2017 in accordance with ASC 810, Consolidation. The Company accounts for its investment in Silver Creek under the equity method of accounting as of December 31, 2018 and 2017.

The Company's consolidated balance sheet as of December 31, 2017 does not include the assets and liabilities of Silver Creek since the Company deconsolidated Silver Creek in the third quarter of 2017. The Company's consolidated statements of operations and comprehensive loss for the year ended December 31, 2017 include Silver Creek's results for the period through July 13, 2017, the day immediately preceding the deconsolidation of Silver Creek.

On August 11, 2017, the Company's stockholders approved an amendment to the Company's certificate of incorporation to effect a one-for-ten reverse stock split of its issued and outstanding common stock (the "Reverse Split"). On September 5, 2017, the Company filed an amendment to its certificate of incorporation to effect the Reverse Split, and on September 6, 2017, the Reverse Split was effective for trading purposes. As a result of the Reverse Split, every ten shares of common stock issued and outstanding was converted into one share of common stock, reducing the number of issued and outstanding shares of common stock from approximately 132.8 million shares to approximately 13.28 million shares. No fractional shares were issued in connection with the Reverse Split. The amendment to the certificate of incorporation also proportionately reduced the number of authorized shares of common stock from 200 million to 20 million. The Reverse Split did not change the par value of the common stock. The Reverse Split did not change the number of authorized shares or par value of the Company's preferred stock, of which there are no shares issued or outstanding. All outstanding stock options and convertible notes entitling their holders to purchase shares of common stock or acquire shares of common stock upon conversion, as the case may be, were adjusted as a result of the Reverse Split, as required by the terms of these securities. This change is reflected throughout the financial statements as appropriate. As a result, all share and per share amounts have been adjusted retroactively to reflect the Reverse Split for all periods. For additional information, see Note 14, "Stock-Based Compensation."

Consolidated Statements of Cash Flows

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the statement of financial position that sum to the total of the same such amounts shown in the statement of cash flows:

(in thousands)	December 31, 2018	December 31, 2017
Cash and cash equivalents	$ 20,079	$ 93,441
Restricted cash (short-term)	584	102
Restricted cash (long-term)	—	674
Total cash, cash equivalents and restricted cash shown in the consolidated statement of cash flows	$ 20,663	$ 94,217

Restricted cash on the statement of financial position for 2018 and 2017 primarily represents amounts pledged as collateral for operating lease obligations as contractually required.

Use of Estimates

GAAP requires the Company's management to make estimates and judgments that may affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures. The Company bases estimates and judgments on historical experience and on various other factors that it believes to be reasonable under the circumstances. The most significant estimates in these consolidated financial statements include, but may not be limited to, accounting for stock-based compensation and the accrual of research and development expenses. The Company's actual results may differ from these estimates under different assumptions or conditions. The Company evaluates its estimates on an ongoing basis. Changes in estimates are reflected in reported results in the period in which they become known by the

Company’s management.

Certain estimates, such as revenue recognition, estimates of discounts and allowances related to commercial sales of ONIVYDE, estimates utilized in the valuation of inventory and useful lives with respect to long-lived assets and intangible assets, related specifically to the Commercial Business, which has been reclassified under discontinued operations.

Cash, Cash Equivalents and Restricted Cash

Cash and cash equivalents are short-term, highly liquid investments with original maturities of three months or less at the date of purchase. Investments qualifying as cash equivalents primarily consist of money market funds, commercial paper, corporate notes and bonds and certificates of deposit.

Cash accounts with any type of restriction are classified as restricted cash. If restrictions are expected to be lifted in the next twelve months, the restricted cash account is classified as current. As of December 31, 2018 and 2017, the Company’s restricted cash of $0.6 million and $0.8 million, respectively, represents amounts pledged as collateral for operating lease obligations as contractually required.

Marketable Securities

Marketable debt securities consist of investments with original maturities greater than 90 days at their acquisition date. The Company classifies all of its marketable debt securities as available-for-sale securities. The Company's marketable debt securities are measured and reported at fair value using quoted prices in active markets for similar securities. Unrealized gains and losses on available-for-sale securities are reported as accumulated other comprehensive loss, which is a separate component of stockholders' equity. The cost of securities sold is determined on a specific identification basis, and realized gains and losses are included in other income and expenses, net in the consolidated statements of operations and comprehensive loss.

The Company evaluates its marketable debt securities with unrealized losses for other-than-temporary impairment. When assessing marketable debt securities for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary," the Company reduces the investment to fair value through a charge to the statement of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

Property and Equipment

Property and equipment, including leasehold improvements, are recorded at cost and depreciated when placed into service using the straight-line method, based on their estimated useful lives as follows:

	Estimated Useful Life
Asset Classification	(in years)
Lab equipment	3 – 7
IT equipment	3 – 7
Leaseholds improvements	Lesser of useful life or lease term
Furniture and fixtures	3 - 7

Costs for capital assets not yet placed into service have been capitalized as construction-in-progress and will be depreciated in accordance with the above guidelines once placed into service. Costs for repairs and maintenance are expensed as incurred, while major betterments are capitalized. The Company capitalizes interest cost incurred on funds used to construct property and equipment. The capitalized interest is recorded as part of the asset to which it relates and is depreciated over the asset's estimated useful life. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is reflected in earnings.

The Company reviews its long-lived assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of assets may not be fully recoverable or that the useful lives of these assets are no longer appropriate. Each impairment test is based on a comparison of the undiscounted cash flow to the recorded value of the asset. If impairment is indicated, the asset will be written down to its estimated fair value on a discounted

cash flow basis.

Accrued Expenses