2019 ANNUAL REPORT

Millendo is **relentlessly pursuing therapies** that alleviate patient suffering due to endocrine diseases

MILLENDO THERAPEUTICS

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 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, 2019

OR

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

Commission File Number: 001-35890

Millendo Therapeutics, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**45-1472564**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
110 Miller Avenue, Suite 100 Ann Arbor, Michigan	**48104**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (734) 845-9000

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

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on which Registered**
Common Stock, $0.001 par value	MLND	The Nasdaq Stock Market, LLC

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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). Yes ☒ No ☐

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

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

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

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

The aggregate market value of the voting and non-voting common equity of the registrant held by non-affiliates as of June 30, 2019 (the last business day of the registrant's most recently completed second fiscal quarter), based on a closing price of $11.56 per share of the registrant's common stock as reported on The Nasdaq Global Market on June 28, 2019, was approximately $124.4 million. For purposes of this computation, all officers, directors, and 10% beneficial owners of the registrant are deemed to be affiliates. Such determination should not be deemed to be an admission that such officers, directors or 10% beneficial owners are, in fact, affiliates of the registrant.

As of March 1, 2020, the registrant had 18,266,545 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for its 2020 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K are incorporated by reference in Part III, Items 10-14 of this Annual Report on Form 10-K.

EXPLANATORY NOTE

On December 7, 2018, OvaScience, Inc., or the Company, completed a reverse merger with what was then known as "Millendo Therapeutics, Inc.", or Private Millendo, in accordance with the terms of the Agreement and Plan of Merger and Reorganization dated as of August 8, 2018, as amended on September 25, 2018 and November 1, 2018, or the Merger Agreement, by and among the Company, Private Millendo and Orion Merger Sub, Inc., a Delaware corporation and a wholly owned subsidiary of the Company, or Merger Sub, pursuant to which, among other matters, Merger Sub merged with and into Private Millendo, with Private Millendo continuing as a wholly owned subsidiary of the Company. We refer to the foregoing transactions in this Annual Report on Form 10-K as "the Merger". On December 6, 2018, in connection with, and prior to the completion of, the Merger, the Company effected a 1-for-15 reverse stock split of its common stock, or the Reverse Stock Split, and immediately following the Merger, the Company changed its name to "Millendo Therapeutics, Inc." Following the completion of the Merger, the business conducted by the Company became the business conducted by Private Millendo, which is a late-stage biopharmaceutical company primarily focused on developing novel treatments for orphan endocrine diseases. All references to common stock share and per share amounts in this Annual Report have been retroactively adjusted to reflect, where applicable, the Reverse Stock Split, as indicated. As used herein, the words "Millendo," "we," "us," and "our" refer to Millendo Therapeutics, Inc. and its direct and indirect subsidiaries, as applicable. In addition, the word "OvaScience" refers to the Company prior to the completion of the Merger.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 1. "Business," Part I, Item 1A. "Risk Factors," and Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations," but are also contained elsewhere in this Annual Report. In some cases, you can identify forward-looking statements by the words "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue" and "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include statements about:

- our plans to develop and commercialize our product candidates;
- the progress and timing of our ongoing and planned clinical trials for our product candidates;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the clinical utility of our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position;
- our plans to in-license, acquire, develop and commercialize additional product candidates;
- our competitive position and the development of and projections relating to our competitors or our industry;
- our ability to identify, recruit and retain key personnel;
- the impact of laws and regulations;
- our plans to identify additional product candidates with significant commercial potential that are consistent with our commercial objectives; and
- our estimates regarding future revenue, if any, future expenses, the funding of our operations, as well as our future capital requirements and needs for additional financing.

You should refer to Item 1A. "Risk Factors" in this Annual Report for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The forward-looking statements in this Annual Report represent our views as of the date of this Annual Report. We anticipate that subsequent events and developments may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report.

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PART I

ITEM 1. BUSINESS

Overview

We are a late-stage biopharmaceutical company primarily focused on developing novel treatments for orphan endocrine diseases where current therapies do not exist or are insufficient. The endocrine system is a collection of glands that secrete hormones into the blood stream to regulate a number of functions, including appetite, metabolism, growth, development and reproduction. Diseases of the endocrine system can cause multiple and varied symptoms, including appetite dysregulation, metabolic dysfunction, obesity, cardiovascular disease, menstrual irregularity, hirsutism, and infertility.

We are currently advancing three product candidates. Our most advanced product candidate, livoletide (AZP-531), is a potential treatment for Prader-Willi syndrome ("PWS"), a rare and complex genetic endocrine disease usually characterized by hyperphagia, or insatiable hunger, that contributes to serious complications, a significant burden on patients and caregivers, and early mortality. In a randomized, double-blind, placebo-controlled Phase 2a clinical trial in 47 patients with PWS, we observed that administration of livoletide once daily was associated with a clinically meaningful improvement in hyperphagia, as well as a reduction in appetite. In a pre-specified analysis of 38 home-resident patients with PWS from the Phase 2a trial, we observed a larger and statistically significant decrease in hyperphagia following administration of livoletide as compared to placebo. In March 2019, we initiated a Phase 2b/3 clinical trial of livoletide in patients with PWS. The randomized, double-blind, placebo-controlled pivotal Phase 2b trial includes 158 patients with PWS ages 8 to 65, recruited across 38 sites in the United States, Europe and Australia. As of February 26, 2020, the three-month "core" period of the Phase 2b trial has been completed. Topline results from the pivotal Phase 2b trial are expected in early second quarter of 2020. A protocol amendment was submitted to the U.S. Food and Drug Administration, or FDA, on August 7, 2019, which allows 4- to 7-year-olds to participate in the Phase 2b/3 clinical trial. We continue to recruit patients in this age group. On July 29, 2019, the FDA designated the investigation of livoletide for PWS as a Fast Track development program. We are also conducting preclinical activities in support of the development of a multi-dose pen device to improve patient and caregiver convenience, as well as patient compliance, and to further simplify the administration of livoletide.

We are developing nevanimibe (ATR-101) as a potential treatment for patients with congenital adrenal hyperplasia ("CAH"), a rare, monogenic adrenal disease that requires lifelong treatment with exogenous cortisol, often at high doses. These chronic high doses of cortisol can result in side effects that include diabetes, obesity, hypertension and psychological problems. When on suboptimal doses of cortisol, female patients with CAH can experience hirsutism, infertility and menstrual irregularity, and male patients with CAH can experience testicular atrophy, infertility and testicular tumors. It is often difficult for physicians to appropriately treat CAH without causing adverse consequences. We reported results from our Phase 2a clinical trial of nevanimibe in patients with CAH in March 2018 and initiated a Phase 2b trial in the third quarter of 2018. We expect to report topline results from the first cohort of the Phase 2b trial in the second half of 2020. Enrollment for the second cohort of the Phase 2b trial is continuing and sites are actively enrolling patients. We expect to provide an additional update on the second cohort in the second half of 2020.

We also have a neurokinin 3 receptor (NK3R) antagonist (MLE-301) in our research and development pipeline, which we plan to develop as a potential treatment of vasomotor symptoms ("VMS"), commonly known as hot flashes and night sweats, in menopausal women. MLE-301 is currently in preclinical studies designed to enable first-in-human clinical studies, which we expect to initiate in the second half of 2020.

We had also been investigating nevanimibe (ATR-101) as a potential treatment for patients with endogenous Cushing's syndrome ("CS"), a rare endocrine disease characterized by excessive cortisol production from the adrenal glands. As a result of slower than anticipated enrollment in our CS Phase 2 clinical trial, we elected to discontinue the trial in August 2019, suspend development of nevanimibe for the treatment of CS, and focus our resources on other programs in our research and development pipeline.

Livoletide (AZP-531) for the treatment of Prader-Willi syndrome (PWS)

We are developing livoletide for the treatment of patients with PWS, a rare and complex genetic endocrine disease affecting appetite, growth, metabolism, cognitive function and behavior. Recognized as the most common genetic cause of life-threatening childhood obesity, PWS is estimated to affect between 8,000 to 11,000 patients in the United States and 13,000 to 18,000 in Europe. While patients with PWS experience a multitude of symptoms, hyperphagia, which typically begins in early childhood, is among the most serious. Hyperphagia begins at an average of eight years old and continues through adulthood. There are approximately 7,000 diagnosed patients with PWS who have hyperphagia in the United States. When coupled with

the low resting energy expenditures that also characterize PWS, hyperphagia often leads to significant weight gain and obesity. Mortality occurs early in patients with PWS, with the average age of death approximately 30 years, coming from respiratory distress, cardiovascular events and accidents, most resulting from complications associated with hyperphagia. There are currently no approved treatments for hyperphagia or the abnormal eating behaviors associated with PWS. Managing hyperphagia requires security measures to prevent access to food in cupboards, refrigerators and garbage, placing a significant burden on patients and their caregivers, often parents. Growth hormone is used in a majority of pediatric patients with PWS to help optimize adult height, cognition and body composition, but it has shown no convincing evidence to date in improving hyperphagia.

We believe that livoletide, a cyclic peptide analogue of unacylated ghrelin, or UAG, may provide a unique approach for the treatment of hyperphagia in patients with PWS by addressing the underlying hormone dysregulation that causes the disease. In a randomized, double-blind, placebo-controlled Phase 2a clinical trial in 47 patients with PWS, we observed that administration of livoletide once daily was associated with a clinically meaningful improvement in hyperphagia, as assessed by the PWS Hyperphagia Questionnaire, as well as a reduction in appetite. In a pre-specified analysis of 38 home-resident patients with PWS from the Phase 2a trial, we observed a larger and statistically significant decrease in hyperphagia following administration of livoletide as compared to placebo. Based on clinical and preclinical data, we believe livoletide has the potential to decrease hyperphagia and negative food-related behaviors, with potential long-term benefits with respect to obesity and its complications. In March 2019, we initiated a Phase 2b/3 clinical trial of livoletide for the treatment of hyperphagia in patients with PWS. The randomized, double-blind, placebo-controlled pivotal Phase 2b trial includes 158 patients with PWS ages 8 to 65, recruited across 38 sites in the United States, Europe and Australia. As of February 26, 2020, the three-month "core" period of the Phase 2b trial has been completed. Topline results from the pivotal Phase 2b trial are expected in early second quarter of 2020. A protocol amendment was submitted to FDA on August 7, 2019, which allows 4- to 7-year-olds to participate in the Phase 2b/3 clinical trial. We continue to recruit patients in this age group. We are also conducting preclinical activities in support of the development of a multi-dose pen device to improve patient and caregiver convenience, as well as patient compliance, and to further simplify the administration of livoletide.

We acquired livoletide in connection with our acquisition of Alizé Pharma SAS, or Alizé, in December 2017. We have received orphan drug designation for livoletide from the FDA, and the European Medicines Agency, or EMA, for the treatment of hyperphagia in patients with PWS. In addition, on July 29, 2019, the FDA designated the investigation of livoletide for PWS as a Fast Track development program. As of December 31, 2019, we owned four issued U.S. patents with respect to livoletide, the earliest of which is not due to expire before 2028 and the latest of which is not due to expire before 2033 excluding any additional term for patent term extension.

Nevanimibe for the treatment of classic congenital adrenal hyperplasia (CAH)

We are developing nevanimibe for the treatment of patients with CAH, a rare, monogenic adrenal disease. CAH is diagnosed at birth through universal screening, occurs in approximately one in 15,000 live births in the United States and is characterized by an inability of the body to produce cortisol naturally. patients with CAH require lifelong treatment with exogenous cortisol, often at high doses, which can result in side effects that include diabetes, obesity, hypertension and psychological problems. Conversely, in the absence of suppressive cortisol levels, excess steroid precursors and androgens are generated and can result in hirsutism, infertility and menstrual irregularity in female patients with CAH, and testicular atrophy and infertility in male patients with CAH. In addition, as many as half of male patients with CAH develop large testicular tumors.

We believe that nevanimibe, a potentially first-in-class acyl coenzyme A: cholesterol acyltransferase 1, or ACAT1, inhibitor represents a novel, adrenal-specific approach to treating CAH that will minimize the need to administer chronic high doses of exogenous cortisol. ACAT1 is a critical enzyme involved in adrenal steroid synthesis and, by inhibiting ACAT1, nevanimibe seeks to suppress the hormonal process that ultimately leads to the production of excess steroid precursors, particularly 17-hydroxyprogesterone, or 17-OHP, and androgens in patients with CAH. In a Phase 2a clinical trial of nevanimibe for the treatment of patients with CAH, we observed nevanimibe to be associated with clear signs of clinical activity in seven of 10 treated patients, as well as to have rapid onset of action. In this trial, we further observed that during treatment with nevanimibe at all doses, patients exhibited a mean reduction in levels of 17-OHP, the key biomarker used by physicians to guide patient treatment, while during administration of placebo, patients exhibited a mean increase in 17-OHP levels. Seventy percent of subjects experienced a decrease in 17-OHP of at least 50% during at least one nevanimibe treatment period. We initiated a Phase 2b clinical trial of nevanimibe in patients with CAH in the third quarter of 2018. We expect to report topline results from the first cohort of the Phase 2b trial in the second half of 2020. Enrollment for the second cohort of the Phase 2b trial is continuing and sites are actively enrolling patients. We expect to provide an additional update on the second cohort in the second half of 2020.

We have received orphan drug designation for nevanimibe from the FDA and the EMA for the treatment of CAH. As of December 31, 2019, we owned two issued U.S. patents with respect to nevanimibe, which are not due to expire before 2035, and we jointly owned, with University of Michigan, three issued U.S. patents, which are each not due to expire before 2033 excluding any additional term for patent term extension.

Neurokinin 3 receptor (NK3R) antagonist for the treatment of vasomotor symptoms (VMS)

We have a neurokinin 3 receptor (NK3R) antagonist (MLE-301) in our research and development pipeline, which we plan to develop as a potential treatment of VMS, commonly known as hot flashes and night sweats, in menopausal women. VMS are experienced by up to 70% of women as they advance through menopause. We believe that approximately 20 million women in the United States experience VMS at any given time and that these patients are motivated to seek medical treatment for relief.

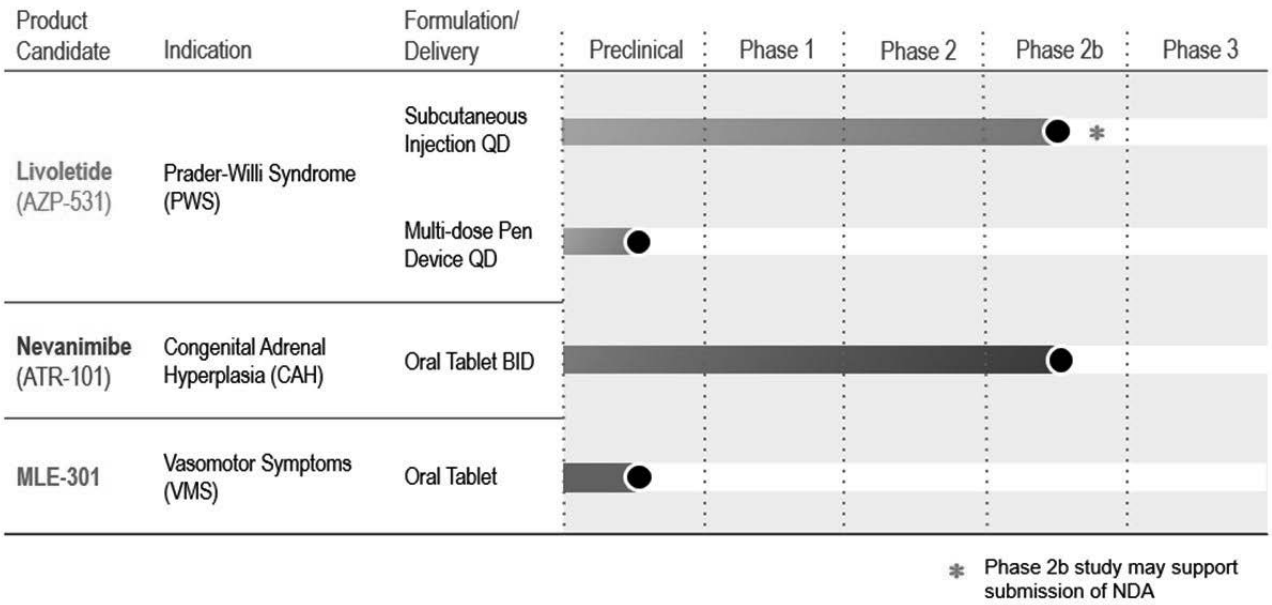
The sensations of heat and/or perspiration associated with VMS can occur frequently, generally last several minutes, and are often preceded or followed by sensations of cold and/or shivering. VMS interfere with the lives of affected women in a number of ways, including disrupting patients' ability to sleep and concentrate and causing anxiety and depression. VMS tend to start in the peri-menopausal period and continue for an average of 7.4 years, according to recent data published in the *Journal of the American Medical Association,* but may last for up to 15 years. Current standards of therapy include hormone replacement therapy, or HRT, Selective Serotonin Reuptake Inhibitors, or SSRIs, and a variety of over-the-counter treatments. NK3R plays a key role in regulating the activity of KNDy (kisspeptin/NKB/dynorphin) neurons, which we believe participate in the generation of VMS. Estrogen is known to be a negative regulator of the KNDy neurons. As estrogen levels fall in peri-menopausal women, the absence of estrogen negative feedback causes the KNDy neurons to become hypertrophic and hyperactive. Hyperactivity of the KNDy neurons is believed to drive the process that causes VMS. By inhibiting the NK3R signaling on the KNDy neurons and potentially other NK3R-expressing neurons that propagate heat dissipation signals through the hypothalamus, MLE-301 aims to reduce the effects of hyperactive KNDy neurons and thereby address the excessive heat dissipation signaling associated with VMS. We believe this approach has the potential to provide a once-daily alternative to HRT for patients with VMS.

MLE-301 is currently in preclinical studies designed to enable first-in-human clinical studies, which we expect to initiate in the second half of 2020.

As of December 31, 2019, we owned one pending U.S. patent application with respect to MLE-301, which, if issued, is not due to expire before 2040, excluding any additional term for patent term adjustment or extension. As of December 31, 2019, we exclusively licensed from Roche one issued U.S. patent with respect to MLE-301, which is not due to expire before 2031, excluding any additional term for patent term adjustment or extension.

Our Pipeline

The figure below depicts our product candidate pipeline:



Strategy

We are a late-stage biopharmaceutical company primarily focused on developing novel treatments for orphan endocrine diseases where current therapies do not exist or are insufficient. Key elements of our strategy are as follows:

- Rapidly and efficiently advance development of, obtain approval for, and commercialize livoletide for the treatment of hyperphagia in patients with PWS. Building on our Phase 2a trial results, we believe livoletide may provide the first treatment to address hyperphagia in patients with PWS, one of the most serious symptoms of the disease and where we believe there is a significant unmet medical need. In March 2019, we initiated a Phase 2b/3 clinical trial of livoletide for the treatment of hyperphagia in patients with PWS. The randomized, double-blind, placebo-controlled pivotal Phase 2b trial includes 158 patients with PWS ages 8 to 65, recruited across 38 sites in the United States, Europe and Australia. As of February 26, 2020, the three-month "core" period of the Phase 2b trial has been completed. Topline results from the pivotal Phase 2b trial are expected in early second quarter of 2020. We believe that the Phase 2b trial, if persuasive statistically, may support the submission of an NDA in the United States or a marketing authorization application in Europe, for livoletide for the treatment of hyperphagia in patients with PWS.

- Pursue development of, obtain approval for, and commercialize nevanimibe for the treatment of CAH. We believe nevanimibe, working through a novel mechanism of action, may allow patients with CAH to obtain therapeutic benefit from exogenous cortisol at lower and better-tolerated doses. In so doing, nevanimibe may enable physicians to effectively treat the disease with lower doses of exogenous cortisol, thereby reducing the effects of long-term high doses of exogenous cortisol, while simultaneously preventing androgen excess. We reported results from our Phase 2a clinical trial of nevanimibe in patients with CAH in March 2018 and initiated a Phase 2b clinical trial in the third quarter of 2018. We expect to report topline results from the first cohort of the Phase 2b trial in the second half of 2020. Enrollment for the second cohort of the Phase 2b trial is continuing and sites are actively enrolling patients. We expect to provide an additional update on the second cohort in the second half of 2020.

- Pursue clinical development of MLE-301 in support of its potential approval as a non-hormonal treatment for VMS in menopausal women. Preclinical studies are underway that are designed to enable first-in-human clinical trials of MLE-301, which we expect to initiate in the second half of 2020. Our approach aims to provide a once-daily alternative to HRT for women with VMS.

- Continue to expand our pipeline by leveraging our expertise in in-licensing and acquiring product candidates. We have a strong track record of licensing and acquiring novel programs to build our current pipeline and we plan to strategically pursue licensing or acquisition of novel therapeutic opportunities that complement our existing portfolio. We believe that there are many opportunities to leverage our deep endocrine expertise to develop new treatments for endocrine diseases with significant unmet medical needs.
- Build a specialized sales and marketing organization in the United States primarily targeting endocrinologists. If approved by the FDA, we plan to commercialize our current orphan endocrine product candidates in the United States ourselves. As we advance livoletide and nevanimibe through clinical development, we plan to grow our commercial organization in support of anticipated product launches.
- Maximize the value of our portfolio by strategically collaborating in selected markets. We currently have worldwide development and commercialization rights with respect to all of our product candidates. We plan to strategically consider collaboration or partnering opportunities in markets outside of the United States. We believe our strategy will allow us to efficiently allocate resources to maximize the commercial potential of our product candidates, if approved.

Product Candidates

Livoletide (AZP-531) for the treatment of Prader-Willi syndrome (PWS)

Background

PWS is a rare endocrine disease caused by a spontaneous genetic error that results in lack of expression of several genes on chromosome 15 and is usually characterized by hyperphagia, intellectual disability, short stature and incomplete sexual development. Recognized as the most common genetic cause of life-threatening childhood obesity, PWS occurs in approximately one in 15,000 births, with an estimated prevalence of 8,000 to 11,000 patients in the United States and 13,000 to 18,000 patients in Europe. Hyperphagia is one of the most serious symptoms of the disease and where we believe there is a significant unmet medical need. Hyperphagia begins at an average of eight years old and continues through adulthood. There are approximately 7,000 diagnosed patients with PWS who have hyperphagia in the United States.

During infancy, patients with PWS often have low muscle tone, or hypotonia, and failure to thrive, which leads to early diagnosis, generally confirmed through genetic testing. Early in childhood, appetite and interest in food start to increase and, by approximately five to eight years of age, patients experience an increase in hyperphagia. PWS then patients typically display aggressive and obsessive food-seeking behaviors, including food storage, foraging and hoarding, all of which represent a lifelong source of distress and severely affect social adaptation, occupational performance and quality of life. In addition, hyperphagia in patients with PWS is associated with significant morbidity, including weight gain and obesity often exacerbated by the low resting energy expenditure levels that characterize the disease, type 2 diabetes and related complications, stomach rupture and choking. More than half of adult patients with PWS have a body mass index over 40 and one quarter of adult patients with PWS have type 2 diabetes. Mortality occurs early in patients with PWS, with the average age of death approximately 30 years, coming from respiratory distress, cardiovascular events and accidents, most resulting from complications associated with hyperphagia.

Most patients with PWS are unable to live independently or work and require constant supervision and care. Managing hyperphagia requires security measures to prevent access to food in cupboards, refrigerators and garbage, placing a significant burden on patients and their caregivers, often parents. Caregivers often struggle to control the aggressive food-seeking behavior of the patients with PWS under their care, especially as patients age and gain weight as a result of the disease. According to the *Foundation for Prader-Willi Research*, 74% of caregivers identified reduced hyperphagia as the most desirable feature they would look for in an ideal PWS treatment, absent a cure. This struggle with food is compounded by the fact that a significant majority of patients with PWS suffer from some form of intellectual or emotional disability, resulting in some patients with PWS ultimately being transferred to a group home setting. There are currently no approved treatments for hyperphagia or the abnormal eating behaviors associated with PWS. Growth hormone is used in a majority of pediatric patients with PWS to help optimize adult height, cognition and body composition, but it has shown no convincing evidence to date in improving hyperphagia.

While the basis for the abnormal eating behavior in patients with PWS is not yet fully understood, evidence suggests involvement of appetite hormone disturbances and dysfunction of the mechanisms of the central nervous system that regulate food intake. Acylated ghrelin, or AG, is the most potent known appetite-stimulating hormone and is commonly known as the "hunger hormone." AG acts in the hypothalamus and plays a central role in the regulation of feeding and food seeking behavior.

Signaling through the AG receptor, also known as the growth hormone secretagogue receptor, has been linked to many physiological functions, including appetite stimulation, lipid accumulation and insulin resistance. Historically, research has linked high total ghrelin concentrations (which includes AG, UAG and other peptide forms of ghrelin) to the hyperphagia and excessive eating that is characteristic of PWS. However, multiple clinical studies of ghrelin-lowering agents in patients with PWS have not shown improvement in appetite or hyperphagia. In contrast, livoletide is a cyclic peptide analogue of UAG - a naturally occurring hormone associated with inhibition of AG-induced food intake, reduction of insulin levels and inhibition of adipose tissue deposition. UAG is also referred to as des-acyl ghrelin, or DAG. The observations from these recent studies suggest a potential role for UAG in negatively regulating hyperphagia.

We believe that livoletide may provide the first treatment to address hyperphagia in patients with PWS by addressing the underlying hormone dysregulation causing the disease.

Clinical development

To date, our livoletide clinical program has included clinical trials with over 300 subjects, including a Phase 1 clinical program with 44 healthy volunteers, 32 overweight or obese adults and 36 type 2 diabetes patients, and a Phase 2a clinical trial with 47 patients with PWS. A Phase 2b/3 clinical trial of livoletide in patients with PWS is ongoing with 158 subjects included in the pivotal Phase 2b trial.

Phase 2b trial

In March 2019, we initiated a Phase 2b/3 clinical trial of livoletide in patients with PWS, which we often refer to as the ZEPHYR trial.

Patients are administered one of two different doses of livoletide based on body weight, or a placebo, by once daily subcutaneous injection. The PWS Hyperphagia Questionnaire, or HQ, is a disease-specific instrument that has been specifically designed and developed to capture food-related behaviors in patients with PWS, as reported by caregivers. The FDA and EMA have accepted a nine-item version of the HQ as the primary endpoint in PWS clinical trials. The primary endpoint of our Phase 2b/3 trial is an assessment of changes in hyperphagia based on this nine-item PWS Hyperphagia Questionnaire for Clinical Trials, or HQ-CT. Secondary endpoints include assessments of changes in total body fat mass, body mass index and body weight. Following completion of the three-month placebo-controlled "core" portion of the trial, patients then continue in a nine-month extension, which we anticipate will provide up to 12 months of safety and efficacy data.

The randomized, double-blind, placebo-controlled pivotal Phase 2b trial includes 158 patients with PWS ages 8 to 65, recruited across 38 sites in the United States, Europe and Australia. These patients had an average baseline HQ-CT score of approximately 20. This baseline HQ-CT score is consistent with the baseline HQ score of approximately 18 in home-resident patients with PWS with a baseline HQ-CT score of 10 or greater, which is consistent with ZEPHYR Phase 2b protocol inclusion criteria. We believe this indicates similar underlying demographics between the Phase 2a trial and the Phase 2b trial population. As of February 26, 2020, the three-month "core" period of the Phase 2b trial has been completed. Of the 158 subjects randomized, 156 subjects successfully completed the three-month endpoint with two subjects of 158 discontinuing during the core period. This represents an approximate 1% drop-out rate for the core period, and the 156 patients who completed the three-month endpoint have all moved into the nine-month extension. Topline results from the pivotal Phase 2b trial are expected in early second quarter of 2020.

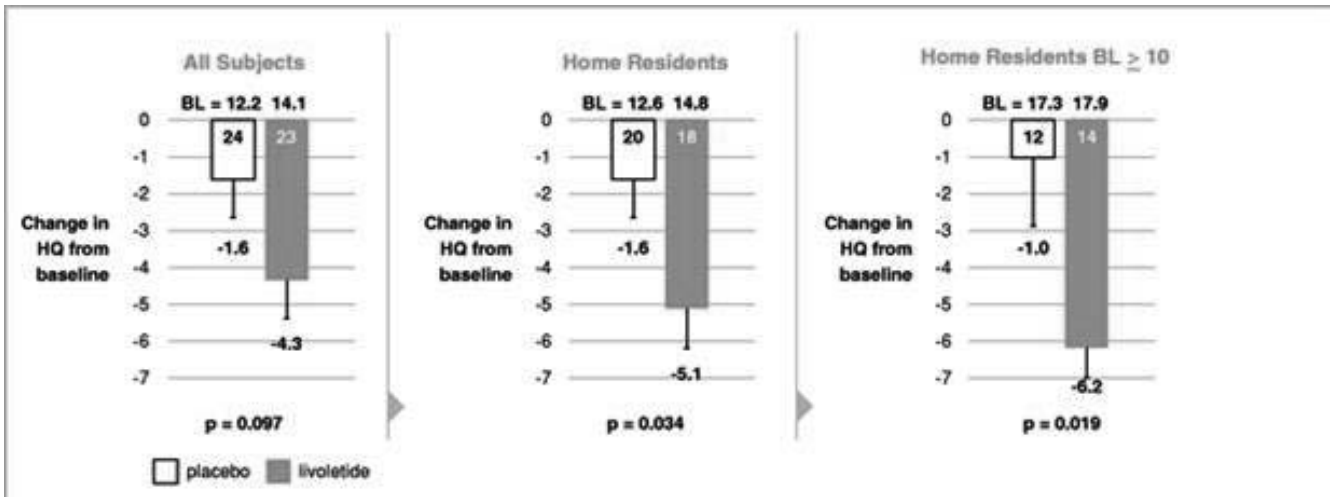
A protocol amendment was submitted to the FDA on August 7, 2019, which allows 4- to 7-year-olds to participate in the Phase 2b/3 clinical trial. We continue to recruit patients in this age group.

We believe that the Phase 2b trial, if persuasive statistically, may support the submission of an NDA in the United States or a marketing authorization application in Europe, for livoletide for the treatment of hyperphagia in patients with PWS.

Phase 2a trial

Livoletide was evaluated in a randomized, double-blind, placebo-controlled Phase 2a clinical trial conducted to study its effects in PWS. The trial enrolled 47 patients with PWS and included both patients residing at home and at a single hospital-based clinical trial site. Patients residing at home were typically cared for by parents, while hospital staff generally cared for patients at the hospital-based site. All patients were administered either a 3 or 4 mg dose of livoletide (based on body weight), or placebo, subcutaneously once daily for 14 days. The primary objective of the trial was to evaluate the safety and tolerability of livoletide over the course of two weeks. The main efficacy variable explored in the trial was changes in hyperphagia, as assessed using the HQ.

In the Phase 2a trial, we observed a decrease in the total HQ score across all patients administered livoletide as compared to placebo (p=0.097). In a pre-specified analysis of 38 home-resident patients with PWS from the Phase 2a trial, we observed a larger and statistically significant decrease in hyperphagia following administration of livoletide as compared to placebo (p=0.034). The analysis of home-resident patients excluded patients residing at the single hospital-based site, which provided a different treatment environment across a number of variables, including more strict controls on access to food and other parameters assessed in the HQ, as well as a lack of consistency with respect to the party completing the HQ. We observed the largest treatment effect in a post-hoc analysis of 26 home-resident patients with baseline HQ scores of 10 or greater, which is reflective of the patient population for our Phase 2b/3 trial. We believe that these changes in HQ scores reflect clinically meaningful changes in hyperphagic behaviors. The figure below shows the change in HQ scores relative to baseline for patients treated with livoletide or placebo, respectively, across each of the three patient groups discussed above:



A result is considered to be statistically significant when the probability of the result occurring by random chance, rather than from the efficacy of the treatment, is sufficiently low. The conventional method for measuring the statistical significance of a result is known as the "p-value," which represents the probability that random chance caused the result (e.g., a p-value = 0.001 means that there is a 0.1% or less probability that the difference between the control group and the treatment group is purely due to random chance). Generally, a p-value less than 0.05 is considered statistically significant, and may be supportive of a finding of efficacy by regulatory authorities. However, regulatory authorities, including the FDA and EMA, do not rely on strict statistical significance thresholds as criteria for marketing approval and maintain the flexibility to evaluate the overall risks and benefits of a treatment.

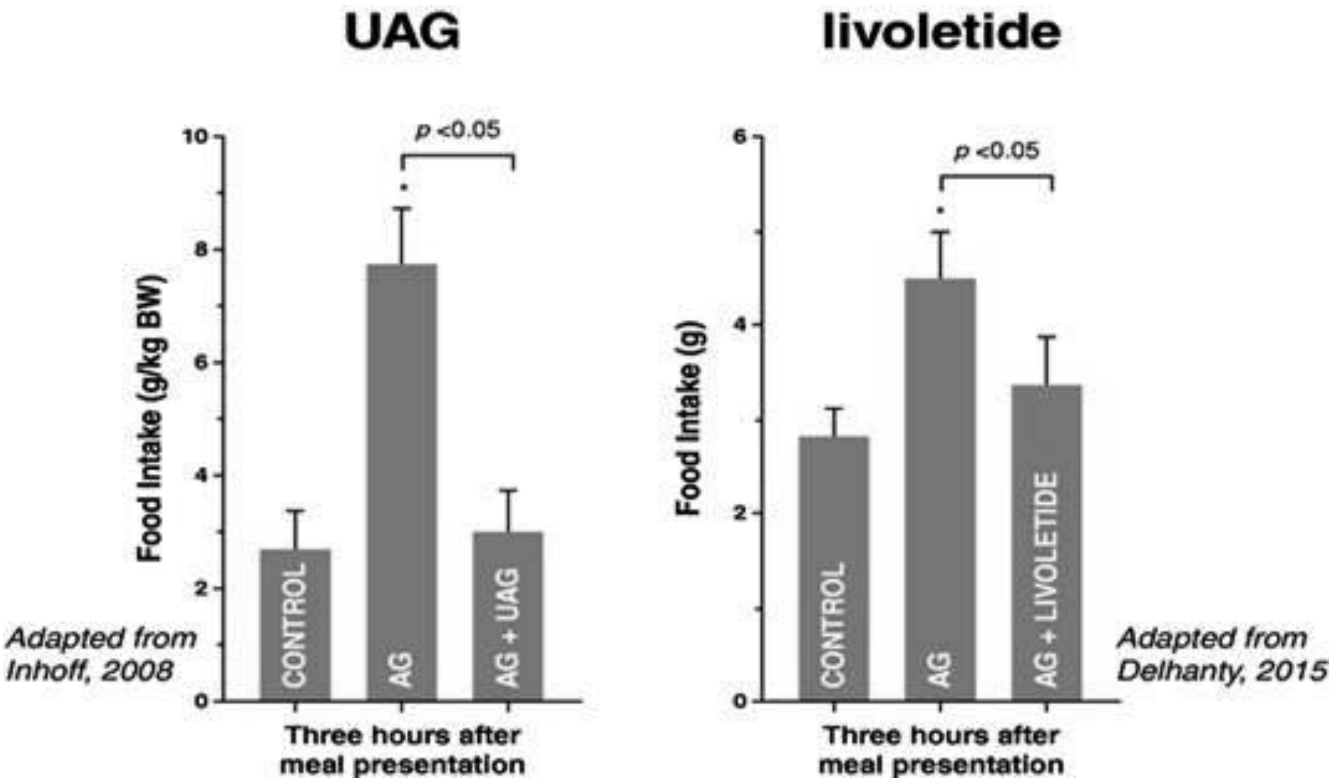
We observed greater decreases in mean values in individual HQ item scores in the livoletide treatment group compared to placebo across each of nine individual questions in the HQ. We believe that improvements in just a few HQ items could have a profound effect on patients and caregivers, including reducing high-risk behaviors. The figure below shows the changes relative to baseline with respect to each of the nine individual items of the HQ in home-resident patients with PWS treated with livoletide and placebo, respectively:

Livoletide was reported to be well tolerated and no serious adverse events were observed. The overall number of reported adverse events were balanced between livoletide and placebo, with 60.9% of patients on livoletide and 58.3% of patients on placebo reporting adverse events. The most commonly reported adverse events in both groups were injection site reactions, which were generally mild and transient. There were no significant changes in vital signs or safety labs, nor were there any premature discontinuations from the trial due to side effects.

Preclinical development

A comprehensive preclinical program for livoletide, including toxicology and pharmacology studies, has been conducted.

In one of a number of preclinical studies in rodents, administration of livoletide was associated with reduced AG-induced food intake. In rodent models of AG-induced food intake, rats receiving an intraperitoneal injection of AG exhibited significantly increased food intake within the first three hours post injection. Co-administration of AG with either UAG or livoletide was associated with inhibition of the stimulatory effect of AG on food uptake over this three-hour period. The figure below shows the observed effects of UAG and livoletide on AG-induced food uptake in rats:



In longer term preclinical studies, overexpression of UAG from a transgene in mice was associated with significantly reduced food intake, fat pad mass, triglycerides and body weight at week 44 following commencement of dosing. These results are consistent with studies of shorter duration in which overexpression of UAG was associated with reduced mouse body weight beginning at age 16 weeks, as well as less development of white adipose tissue and better modulation of glucose tolerance and insulin sensitivity. Administration of livoletide was associated with similar outcomes in a four-week preclinical study.

Based on clinical and preclinical data, we believe that administration of livoletide has the potential to increase functional UAG levels (level of UAG plus livoletide) and decrease hyperphagia and negative food-related behaviors in patients with PWS, with potential long-term benefits with respect to obesity and its complications.

Clinical development plan

We intend to initiate the Phase 3 study that is part of the Phase 2b/3 ZEPHYR protocol following topline results from the Phase 2b study. The number of patients with PWS to enroll in the Phase 3 clinical trial will depend upon the results from the pivotal Phase 2b clinical trial of livoletide in patients with PWS. Patients who participated in the Phase 2b trial will not be eligible to participate in the Phase 3 trial. Patients in the Phase 3 trial will be administered a dose of livoletide (selected on the basis of the Phase 2b results) based on body weight, or a placebo, subcutaneously once daily for six months. The primary endpoint of the trial will be an assessment of changes in hyperphagia based on the HQ-CT. Secondary endpoints include assessments of changes in total body fat mass, body mass index and body weight, subject to change based on the outcome of the pivotal Phase 2b trial. Following completion of the six month placebo-controlled portion of the trial, patients then continue in a six-month extension.

Regulatory

We discussed the development strategy with both the FDA and EMA in advance of initiating the Phase 2b/3 clinical trial with livoletide. There was agreement with key elements of the development program:

- Suitability of the validated nine-item PWS Hyperphagia Questionnaire (HQ-CT) for clinical trials survey as the primary efficacy endpoint for the trial.
- The pivotal Phase 2b trial, if persuasive statistically, may support the submission of an NDA in the United States or a marketing authorization application in Europe, for livoletide for the treatment of hyperphagia in patients with PWS. Additionally, the FDA may require additional data (for example, in younger children) in order to support an NDA approval in PWS in the United States.
- The preference from the FDA to use fixed-exposure dosing (rather than fixed-dosing) given the wide range of body weights to be studied.

Multi-dose pen

While our current clinical development program for livoletide for the treatment of hyperphagia in patients with PWS involves the use of once-daily subcutaneous injections for administration, we are also conducting preclinical activities in support of the development of a multi-dose pen device to improve patient and caregiver convenience, as well as patient compliance, and to further simplify the administration of livoletide.

Nevanimibe for the treatment of classic congenital adrenal hyperplasia (CAH)

Background

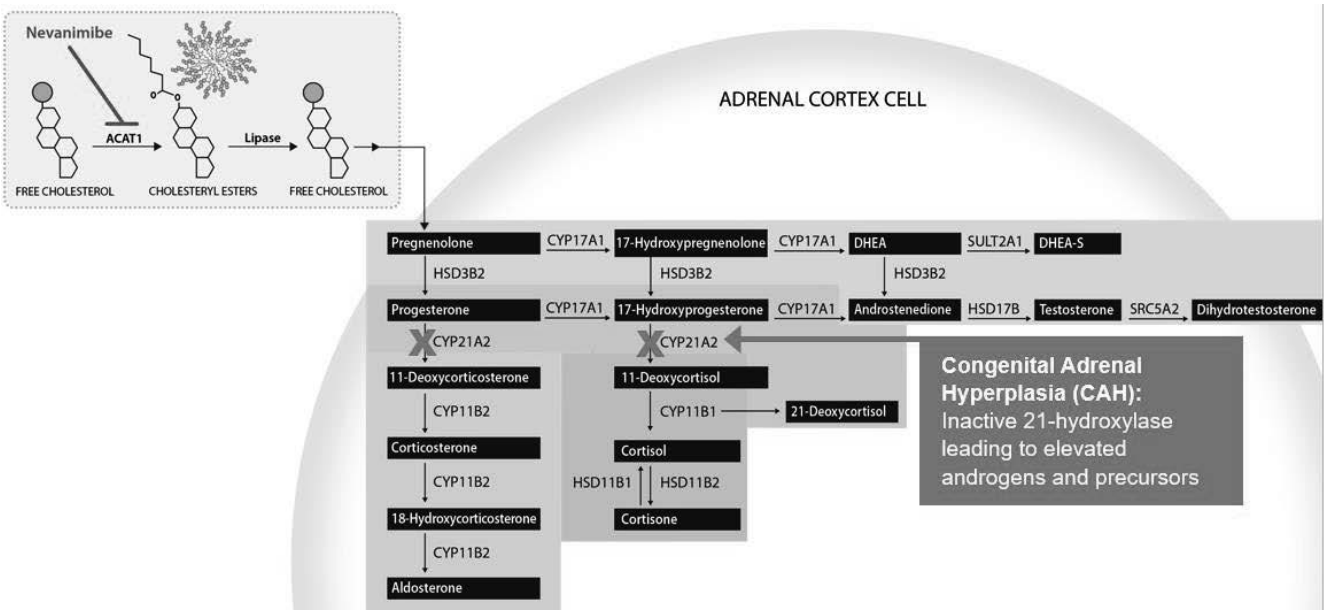
CAH is a rare, monogenic adrenal disease, which results in patients' inability to produce cortisol, excessive production of steroid precursors and androgens, and requires lifelong treatment with exogenous cortisol. CAH occurs in approximately one in 15,000 live births in the United States and has a higher incidence in Europe, with an estimated prevalence of 15,000 to 18,000 patients in the United States and approximately 40,000 patients in Europe. CAH is diagnosed at birth through universal screening.

The most frequent form of CAH, responsible for between 90% and 95% of cases, is caused by a deficiency in the enzyme 21-hydroxylase, which is required for the production of cortisol and other steroids in the adrenal cortex. As the hypothalamus and pituitary gland function normally in patients with CAH, low or nonexistent cortisol levels stimulate the hypothalamus to produce and secrete an excess of corticotropin-releasing hormone, or CRH. Excess CRH stimulates cells in the pituitary gland to produce and secrete excess adrenocorticotropic hormone, or ACTH. In individuals without CAH, excess ACTH would lead to the over-synthesis of cortisol. However, in patients with CAH, the lack of necessary enzymes for cortisol production results in increased levels of the adrenal steroid hormone precursors, including 17-OHP, with approximately 80% of patients with CAH having 17-OHP levels outside of normal bounds. These excess precursors are diverted largely to the androgen pathway, resulting in elevated androgen levels, which leads to hirsutism, virilization, infertility and menstrual irregularity in women. In men, testicular tumors of adrenal gland origin are common.

CAH requires treatment with exogenous cortisol, often at high doses, which both replaces the lack of endogenous cortisol and aims to suppress the hormonal processes that lead to excess CRH, ACTH and androgens. These chronic high doses of cortisol can result in side effects that include diabetes, obesity, hypertension and psychological problems. It is often difficult for physicians to appropriately treat CAH without causing adverse consequences. Few patients with CAH are able to achieve an optimal balance between exogenous cortisol dose and suppression of CRH, ACTH and androgens.

Nevanimibe is an adrenal-selective inhibitor of ACAT1. ACAT1 is a critical enzyme that converts free cholesterol into cholesteryl esters in the adrenal glands. Cholesteryl esters are the reservoirs in which cholesterol is stored prior to its synthesis into adrenal steroids, including cortisol and androgens. By inhibiting ACAT1 in the adrenal glands, nevanimibe seeks to reduce the amount of cholesteryl esters and associated stored cholesterol available for synthesis into adrenal steroids thus reducing the levels of all adrenal steroids. By inhibiting ACAT1, we believe that nevanimibe represents a novel, adrenal-specific approach to treating CAH that will minimize the need to administer chronic high doses of exogenous cortisol to suppress the hormonal process that ultimately leads to the production of excess CRH, ACTH and androgens and precursors, including 17-OHP, in patients with CAH.

The graphic below depicts the mechanism of action of nevanimibe for the treatment of CAH:



Clinical development

Phase 2b trial

The Phase 2b clinical trial of nevanimibe for the treatment of CAH began in the third quarter of 2018 and is ongoing. The Phase 2b trial includes two distinct cohorts of patients. The first cohort includes patients with a baseline 17-hydroxyprogesterone (17-OHP) level, a key measure of disease control, of greater than or equal to 4-times the upper limit of normal (ULN) which is similar to the Phase 2a study population but now with longer duration of treatment and with the ability for additional dose-ranging. The second cohort includes patients with elevated glucocorticoids and a baseline 17-OHP level of less than 4-times ULN. Patients in the second cohort will have their glucocorticoid dose reduced, with an anticipated increase in 17-OHP levels and then treatment with nevanimibe seeking to reduce the 17-OHP levels.

We expect that the open-label, intra-subject dose-escalation trial will enroll a total of 10 or more patients with CAH for each cohort, across approximately 10 to 12 sites.

The trial was initially designed for patients to receive nevanimibe for a total of 12 consecutive weeks starting at a dose of 1000 mg BID. As we previously announced, we submitted a protocol amendment to the appropriate regulatory authorities in all countries with active clinical trial sites to reflect a change in dosing (reducing the starting dose from 1000 mg BID to 500 mg BID) aimed at improving tolerability and an extension of the length of the trial treatment period (from 12 weeks to 16 weeks) to permit dose escalation.

Independent of the starting dose, dose escalation to 1500 mg BID or 2000 mg BID will be based on the primary outcome measure: 17-OHP levels. The primary endpoint will be an assessment of the percentage of patients that achieve 17-OHP levels less than or equal to two times ULN. Secondary endpoints include assessments of levels of other adrenal hormones, including androgens.

We expect to report topline results from the first cohort of the Phase 2b study in the second half of 2020. Enrollment for the second cohort of the Phase 2b trial is continuing and sites are actively enrolling patients. As expected for this second cohort, establishing an appropriate baseline in accordance with the Phase 2 trial protocol takes longer than for the first cohort as exogenous glucocorticoids require adjustment and 17-OHP levels need time to stabilize after these adjustments before initiating treatment with nevanimibe. We expect to provide an additional update on the second cohort in the second half of 2020.

Phase 2a trial

We evaluated nevanimibe in a multicenter, single-blind, intra-patient dose escalation Phase 2a clinical trial for the treatment of adult CAH. The trial's objectives were to evaluate the efficacy and safety of nevanimibe in this patient population.

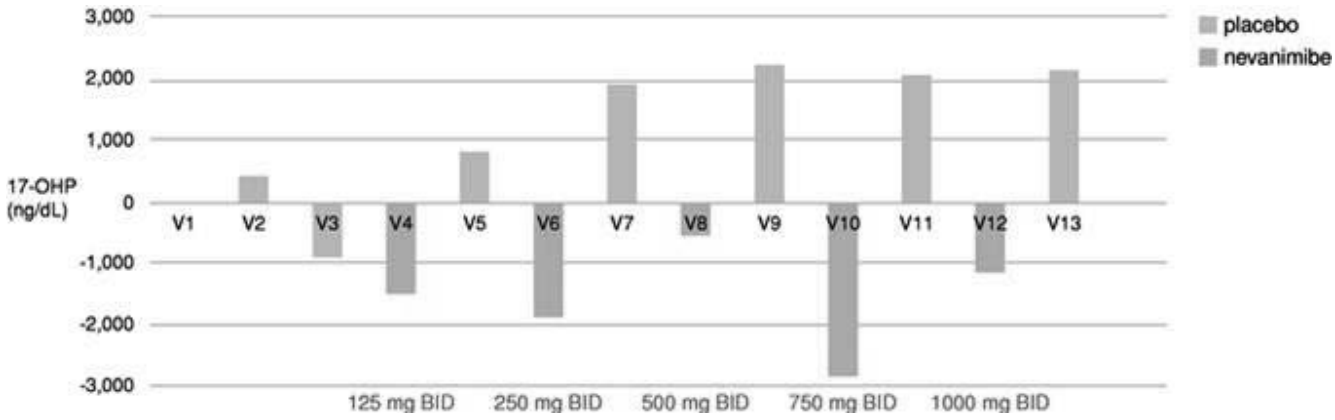
Following a two-week placebo lead-in period, eligible patients with baseline 17-OHP levels greater than or equal to 4-times the upper limit of normal, or ULN, received the lowest dose of nevanimibe for two weeks. This two-week treatment period was followed immediately by a single-blind placebo washout period of two weeks. If the primary outcome measure of reducing 17-OHP levels to less than or equal to 2-times the ULN was not met, the patient was up-titrated to the next highest dose of nevanimibe. This process was repeated until the primary outcome measure was met or the patient reached the highest dose. A total of five nevanimibe dose levels were tested (125 mg BID, 250 mg BID, 500 mg BID, 750 mg BID and 1,000 mg BID). All patients remained on mineralocorticoid and glucocorticoid replacement throughout the trial.

The trial enrolled 10 patients. The baseline 17-OHP levels of patients at screening ranged from seven to 187 times ULN, with a mean value of 52.5 times ULN. Nine patients completed the trial and one patient discontinued from the trial while on the highest dose level of nevanimibe due to a serious adverse event of enteritis.

In the trial, we observed nevanimibe to be associated with clear signs of clinical activity in seven of 10 treated patients. We further observed that during treatment with nevanimibe at all doses, patients exhibited a mean reduction in levels of 17-OHP, while during administration of placebo, patients experienced a mean increase in 17-OHP levels. Two patients met the primary endpoint, with observed 17-OHP reductions to two times the ULN or less, and other patients had observed maximal decreases in 17-OHP of up to 72% during the two week treatment period. Overall, 70% of patients saw a 17-OHP reduction of 50% or more. During the placebo washout periods following each nevanimibe dose level, we observed that 17-OHP increased markedly, with no patients having a mean percentage decrease in 17-OHP. The bar graph below shows the change in the study population mean 17-OHP (ng/dL) values by study visit. Visits are numbered 1 to 13. Visit 1 was the screening visit and is not associated with a change in 17-OHP. The 17-OHP value presented at visit 2 shows the mean change in 17-OHP from visit 1 to the start of the single-blind, two week placebo lead-in period (visit 2). Visit 3 shows the change in 17-OHP that occurred from the start of the single-blind, two week placebo lead-in period (visit 2) to the end of that period (visit 3). We believe that the decrease in 17-OHP associated with visit 3 reflects increased compliance with exogenous cortisol. Visit 4 shows the decrease associated with administration of nevanimibe 125 mg BID, with the mean 17-OHP value at visit 3 serving as the baseline for the two-week nevanimibe 125 mg BID treatment period that ends at visit 4. Visit 5 shows the increase in 17-OHP associated with the two-week placebo washout period that immediately followed the nevanimibe 125 mg BID dosing period, with the mean 17-OHP value at visit 4 serving as the baseline for the two-week placebo period that ends at visit 5. Visits 5 and 6 (where nevanimibe, 250 mg BID was assessed), visits 7 and 8 (where nevanimibe 500 mg BID was assessed), visits 9 and 10 (where nevanimibe, 750 mg BID was assessed) and visits 11 and 12 (where nevanimibe 1,000 mg BID was assessed) followed the same paradigm.

Data with respect to one patient who completed the trial is excluded from the graphic below because that patient was administered high doses of exogenous cortisol in response to a serious adverse event (viral gastroenteritis), which would confound the results of the trial. In addition, one patient met the primary endpoint of the trial following visit 7 and therefore did not receive additional doses of nevanimibe. Accordingly, the graphics below includes data with respect to nine patients through visit seven and eight patients through all 13 visits.

The graphic below illustrates the mean change in 17-OHP levels in patients at the indicated points in time.



We believe the observed decreases in 17-OHP associated with each nevanimibe dose level and the corresponding observed increases in 17-OHP during the placebo wash-out periods demonstrate a treatment effect. We believe signs of clinical activity observed in seven of 10 patients, with two patients meeting the primary endpoint, provide sufficient evidence for the use of nevanimibe in the treatment of CAH to support further development. The primary efficacy endpoint assessed the percentage of patients meeting the primary outcome measure (17-OHP levels less than 2-times ULN); however the relatively small sample size and open-label, intra-subject dose escalation design of the trial precluded the use of formal statistical analyses (e.g., p-values) for either the primary efficacy endpoint or secondary objectives, which included assessments of changes in levels of adreno cortical steroids and steroid intermediates, changes in levels of ACTH and pharmacokinetics.

Nevanimibe was reported to be well tolerated at all dose levels. Two serious adverse events were reported in the trial, both occurring in the same patient: one case of viral gastroenteritis, which was deemed not to be drug related, and one case of enteritis, which was deemed to be drug related. Both serious adverse events were treated with higher than usual doses of exogenous cortisol. The overall number of reported adverse events was balanced between nevanimibe and placebo treatment periods. The most commonly reported adverse events in both treatment periods were gastrointestinal disorders, nasopharyngitis and headaches, which were generally mild and transient. There were no observed dose-related trends in adverse events or safety laboratory results.

Phase 1 trial

We previously studied nevanimibe in a Phase 1 clinical trial in 63 patients with adrenocortical carcinoma across 14 dose-ranging cohorts. In the trial, we observed nevanimibe to be well tolerated at doses up to 158.5 mg/kg/day (approximately 12,000 mg/day for a 75 kg individual). The longest duration of treatment was 13 months (97.9 mg/kg/day). 48 of the patients received a nevanimibe dose similar to or greater than the dose range in our Phase 2b CAH clinical trial.

Preclinical development

A comprehensive preclinical program for nevanimibe, including chronic toxicology and pharmacology studies, has been conducted.

In one of a number of preclinical studies in dogs, we observed that administration of nevanimibe was associated with decreases in levels of adrenal steroids and steroid precursors. Nevanimibe was observed to be associated with dose and time-dependent decreases in basal and ACTH-stimulated levels of all adrenal steroids and steroid precursors tested after 14 days of treatment as shown in the figure below. Notably, both basal and ACTH-stimulated levels of 17-OHP were reduced by 100%.

		% Change after 14d nevanimibe			
Pathway	**Steroid**	**Basal**		**ACTH-Stim**	
Androgen/Estrogen	**Pregnenolone**	80.3	*	78.8	*
	DHEA	51.7		43.3	**
	DHEA-S	99.8		100	
	Androstenedione	77.5		87.3	
	Testosterone	66.6		41.4	
Progesterone	**Progesterone**	88.2	*	84.4	
	17-Hydroxyprogesterone	100		100	
Mineralocorticoid	**11-Deoxycorticosterone**	67.3		86.1	
	Corticosterone	49.5		86.5	
Glucocorticoid	**11-Deoxycortisol**	11.2		77.5	
	Cortisol	32.3		71.4	
	Cortisone	19.2		44.1	

* Day 1 data used for maximum levels
** Day 3 data used for maximum levels

Chronic toxicology studies of nevanimibe in rats and dogs are complete.

Neurokinin 3 receptor (NK3R) antagonist for the treatment of vasomotor symptoms (VMS)

Background

VMS, commonly known as hot flashes and night sweats, in menopausal women, are experienced by up to 70% of women as they advance through menopause. We believe that approximately 20 million women in the United States experience VMS at any given time. VMS interfere with the lives of affected women in a number of ways, including disrupting patients' ability to sleep and concentrate as well as increasing the risk of anxiety and depression. VMS tend to start in the peri-menopausal period and continue for an average of 7.4 years, according to recent data published in the *Journal of the American Medical Association*. In some women, VMS may last for up to 15 years. Current standards of therapy include HRT, SSRIs, and a variety of over-the-counter treatments. While HRT is effective in treating VMS in post-menopausal women, its use and recommended duration thereof is limited by the need for individualized benefit-to-risk assessments of potential increased risk of cardiovascular disease, stroke, deep vein thrombosis, and dementia.

MLE-301 is a selective antagonist of the NK3R, a target that plays a key role in regulating the activity of KNDy (kisspeptin/NKB/dynorphin) neurons, which we believe participate in the generation of VMS. Estrogen is known to be a negative regulator of the KNDy neurons. As estrogen levels fall in peri-menopausal women, the absence of estrogen negative feedback causes the KNDy neurons to become hypertrophic and hyperactive. Hyperactivity of the KNDy neurons is believed to drive the processes that cause VMS. By inhibiting the NK3R signaling on the KNDy neurons and potentially other NK3R-expressing neurons that propagate heat dissipation signals through the hypothalamus, MLE-301 aims to reduce the effects of hyperactive KNDy neurons and thereby address the excessive heat dissipation signaling associated with VMS. We believe this approach has the potential to provide a once-daily alternative to HRT for patients with VMS.

Preclinical development

Preclinical safety assessments for MLE-301, including repeat-dose toxicology and pharmacology studies, are currently being conducted. We expect to initiate first-in-human clinical studies in the second half of 2020.

Sales and Marketing

We have worldwide development and commercialization rights with respect to all of our current product candidates.

If approved by the FDA, we plan to commercialize our current orphan endocrine product candidates in the United States ourselves. As we advance livoletide and nevanimibe through clinical development, we plan to grow our commercial organization in support of anticipated product launches. We intend to build a small, specialized sales force to market livoletide and nevanimibe primarily targeting endocrinologists. We intend to focus on patient support and reimbursement assistance in order to facilitate patient access, uptake and compliance for all indications. We also intend to develop health economic models demonstrating the value of livoletide and nevanimibe to third-party payors.

Outside of the United States, we plan to strategically consider collaboration or partnering opportunities to allow us to efficiently allocate resources to maximize the commercial potential of our product candidates, if approved.

Research and Development

We believe that there are many opportunities to leverage our deep endocrine expertise to develop new treatments for endocrine diseases with significant unmet medical needs. We will continue to seek research and development synergies across all our programs and indications. We also plan to aggressively pursue licensing or acquisitions of novel therapeutic opportunities exploiting biological discoveries that can transform the treatment of endocrine diseases.

Assignment Agreement with Erasmus University Medical Center and the University of Turin

We have an assignment agreement with Erasmus University Medical Center, the University of Turin and certain individuals, which we refer to collectively as the assignors, for certain patents and patent applications relating to livoletide.

In connection with the assignment agreement, we agreed to pay the assignors a flat, low single digit royalty on net commercial sales of products containing livoletide that are covered by the claims of the assigned intellectual property. Further, upon approval of livoletide by the FDA or EMA, we are required to pay the assignors CDN$100,000, which amount will be deducted from any future royalty payments due to the assignors. We also agreed to pay the assignors a low single digit percentage of any

amounts received in connection with our license of the assigned intellectual property or products containing livoletide that are covered by the claims of the assigned intellectual property.

The assignors have a right to repurchase the assigned intellectual property at a certain price in the event we do not, upon receiving notice, use reasonable efforts to develop, introduce for sale and promote products derived from the assigned intellectual property. Such reasonable efforts involve spending an annual amount of at least CDN$100,000 in research and development related to livoletide, actively pursuing the registration, licenses and permits necessary to market livoletide, and the actual commercialization of livoletide, if approved. In addition, pursuant to the assignment agreement, certain individuals at the Erasmus University Medical Center and the University of Turin were granted non-exclusive rights to use the assigned intellectual property for non-commercial research with our prior written consent.

License Agreement with the University of Michigan

In June 2013, we entered into a license agreement with the University of Michigan, or the UM License Agreement, for a worldwide, exclusive, sublicensable license to the University of Michigan's interest in certain patent rights jointly owned with us, covering, among other things, the use of nevanimibe to treat CAH. Such license rights allow us to make, have made, import, export, use, market, offer for sale and sell products containing nevanimibe for such use in the United States. Under the UM License Agreement, the University of Michigan reserved the right to practice the licensed patent rights for its own internal research, public service and internal educational purposes and to grant such rights to other non-profit research institutions solely for its internal use.

The UM License Agreement requires that products containing nevanimibe that are used or sold in the United States must be manufactured substantially in the United States. The UM License Agreement further obligates us to use commercially reasonable efforts to bring at least one product containing nevanimibe subject to the licensed rights to market, and to continue active, diligent marketing efforts using commercially reasonable efforts for any such product that achieves regulatory approval throughout the term of the UM License Agreement. We are further obligated under the UM License Agreement to use commercially reasonable efforts to obtain and retain any necessary governmental approvals that are required to manufacture and/or sell products containing nevanimibe that are subject to the licensed patents.

We agreed under the UM License Agreement to use commercially reasonably efforts to reach certain commercialization, research and development milestones by certain dates. We have the right to extend by a specified period the time it takes to achieve such commercialization, research and development milestones upon notice and payment to the University of Michigan of a low six figure fee. We may exercise such right up to a specified number of times during the term of the UM License Agreement. To date, we have exercised this option one time.

As consideration for the rights granted to us under the UM License Agreement, we agreed to pay the University of Michigan a flat, low single figure royalty on net sales of product containing nevanimibe that are covered by the claims of the licensed patents, with minimum royalties per year ranging between $10,000 and $20,000 through 2023 and minimum royalties per year of $0.2 million beginning in 2024 through expiration of the term of the UM License Agreement. We also agreed to make payments to the University of Michigan totaling up to $2.5 million upon the achievement of certain development and commercial milestones. No amounts were paid in 2018 or 2019 related to the achievement of development or commercial milestones. During the year ended December 31, 2019, $0.1 million was paid in order to extend the milestone achievement date of certain development milestones.

We have also agreed to pay a tiered percentage of revenues, other than revenues based on net sales, received under a sublicense of the rights granted under the UM License Agreement. Such revenue percentages range from a mid-single digit to low double digits depending on the stage of development of nevanimibe at the time of the applicable sublicense, with the lower percentages applicable to sublicenses granted at later stages of development.

The UM License Agreement will expire upon expiration of the last to expire of the issued patents that are the subject of the UM License Agreement that would be infringed by our making, having made, using, marketing, importing, exporting, offering to sell and selling of products containing nevanimibe. We may terminate the UM License Agreement upon 90 days' notice. The University of Michigan may terminate the UM License Agreement for any uncured failure to pay amounts due the University of Michigan or for any other uncured material breach, which includes our failure to exercise commercially reasonable efforts to meet research and development milestones by certain deadlines, and if we challenge the validity or enforceability of the licensed patents.

License Agreement with Roche

On October 16, 2018, we entered into a license agreement with F. Hoffmann-La Roche Ltd and Hoffman-La Roche Inc. (collectively, "Roche"), for a worldwide, exclusive license to Roche's interest in certain patent rights and know-how covering, among other things, the use of a neurokinin 3 receptor antagonist (the "Roche License Agreement"). Such license rights allow us to research, have researched, develop, have developed, register, have registered, use, have used, make, have made, import, have imported, export, have exported, market, have marketed, distribute, have distributed, sell and have sold an NK3R antagonist for use in all countries in the world and for all other uses other than diagnostic use. Under the Roche License Agreement, Roche reserved the right to use the NK3R antagonist for internal research purposes.

The Roche License Agreement obligates us to use commercially reasonable efforts to bring at least one product containing the NK3R antagonist subject to the licensed rights to market. We also agreed under the Roche License Agreement to use commercially reasonably efforts to reach certain commercialization, research and development milestones by certain dates.

As consideration for the rights granted to us under the Roche License Agreement, we agreed to pay Roche an up-front payment. Under the terms of the Roche License Agreement, we are also obligated to make significant milestone and royalty payments in connection with the attainment of certain development steps and the sale of resulting products with respect to the NK3R antagonist. No amounts were paid in 2018 or 2019 related to the achievement of development or commercial milestones. In addition, we are required to share a portion of any net proceeds received in connection with certain agreements that we may enter into with third parties to develop and commercialize the NK3R antagonist.

The Roche License Agreement expires on the date when no royalty or other payment obligations under the agreement are or will become due. Prior to the first commercial sale of a product, we may terminate the Roche License Agreement upon three months' notice and, after the first commercial sale of a product, we may terminate the Roche License Agreement upon seven months' notice. Either party may terminate the Roche License Agreement if the other party becomes insolvent breaches any of its material obligations under the agreement, subject to any applicable cure periods.

Competition

The commercialization of new drugs is competitive, and we may face worldwide competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies and ultimately generic companies. Our competitors may develop or market therapies that are more effective, safer or less costly than any that we are commercializing, or may obtain regulatory or reimbursement approval for their therapies more rapidly than we may obtain approval for ours.

With respect to our efforts to treat patients with PWS, livoletide is the only UAG analogue in development. Compounds with several different mechanisms are in clinical development by others for the treatment of hyperphagia in patients with PWS. We are aware of three companies conducting clinical trials seeking to address hyperphagia in patients with PWS. Soleno Therapeutics, Inc. is currently developing diazoxide choline controlled release, an ATP-sensitive potassium channel agonist, and Levo Therapeutics, Inc. is pursuing development of carbetocin, a long-acting analogue of oxytocin. Saniona AB has also announced results of a Phase 2a study in adolescents and adults in PWS for the treatment of hyperphagia. There are also a number of compounds in preclinical development.

We are aware of three other companies developing treatments for patients with CAH: Diurnal Group PLC is developing an exogenous cortisol treatment with a modified release intended to more closely match the physiological release profile of cortisol but recently announced a failed Phase 3 study and placed their United States development activities on hold. Diurnal Group PLC submitted a Market Authorization Application to the EMA in December of 2019. Both Spruce Biosciences, Inc and Neurocrine Biosciences, Inc. are developing CRF1 antagonists and have completed Phase 2 studies in adults with CAH. Neurocrine Biosciences, Inc. has announced the initiation of a Phase 2 study in a pediatric CAH population and announced their intention to start an adult Phase 3 CAH study in mid-2020. Spruce Biosciences has announced intentions to conduct two Phase 2b studies in adults with CAH as well as initiate a pediatric Phase 2 study. BridgeBio Pharma, Inc. is evaluating a gene therapy program (BBP-631) to treat CAH and has announced plans to file an IND in 2020.

We are aware of four competing NK3R antagonists currently in clinical development for VMS. Astellas is developing fezolinetant and has announced the initiation of their Phase 3 VMS program. KaNDy Therapeutics has recently announced preliminary positive topline data for NT-814, a dual NK1/3 receptor antagonist, with full trial results yet to be disclosed. Sojournix is currently studying SJX-653 in a Phase 2 trial. Additionally, Acer Therapeutics has announced their intentions to develop osanetant, an NK3R antagonist, for induced vasomotor symptoms stemming from hormonal therapies used to treat breast and prostate cancer.

Intellectual Property

Our success will significantly depend upon our ability to obtain and maintain patent and other intellectual property and proprietary protection for our drug candidates in the United States and internationally, including composition-of-matter, dosage and formulation patents, as well as patent and other intellectual property and proprietary protection for our novel biological discoveries and other important technology inventions and know-how. In addition to patents, we rely upon unpatented trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees as well as selected commercial partners and consultants. Despite these measures, any of our intellectual property and proprietary rights could be challenged, invalidated, circumvented, infringed or misappropriated, or such intellectual property and proprietary rights may not be sufficient to permit us to take advantage of current market trends or otherwise to provide competitive advantages. In addition, such confidentiality agreements and invention assignment agreements can be breached and we may not have adequate remedies for any such breach. For more information, please see "*Risk Factors—Risks Related to Our Intellectual Property*."

We seek patent protection in significant markets and/or countries for each drug in development. We also seek to maximize patent term. The patent exclusivity period for a drug will prevent generic drugs from entering the market. Patent exclusivity depends on a number of factors including the strength of the claims, the initial patent term, patent term adjustments and available patent term extensions based upon delays caused by the regulatory approval process.

The patent positions of biotechnology companies like ours are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our product candidates. As of December 31, 2019, with respect to livoletide patent rights, we owned four issued U.S. patents, one pending U.S. patent application, and a number of patents and pending patent applications in other jurisdictions. As of December 31, 2019, with respect to nevanimibe patent rights, we owned two issued U.S. patents, two pending U.S. patent applications, and a number of pending patent applications in other jurisdictions, and we jointly owned, with University of Michigan, three issued U.S. patents, one pending U.S. patent application, and a number of patent applications in other jurisdictions. As of December 31, 2019, with respect to MLE-301 patent rights, we owned one pending U.S. patent application, and we exclusively licensed from Roche one issued U.S. patent and a number of patents and pending patent applications in other jurisdictions.

We cannot predict whether the patent applications we pursue will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide any proprietary protection from competitors. The patent portfolios for our leading product candidates as of December 31, 2019 are summarized below.

Livoletide

With respect to livoletide patent rights, as of December 31, 2019, we owned four issued U.S. patents, which are not due to expire before 2028, 2028, 2029, and 2033, respectively, excluding any additional term for patent term extension pursuant to the Hatch-Waxman Act; one pending U.S. patent application, which is not due to expire before 2034, excluding any additional term for patent term adjustment or extension; and a number of patent applications in other jurisdictions. The foregoing patents and patent applications cover a form of and methods of making and using livoletide or its analogs. Related international patent applications have issued in Australia, Canada, China, Europe, Japan, and Mexico and are pending in a number of other countries, including Canada, Europe, and India.

Nevanimibe

With respect to nevanimibe patent rights, as of December 31, 2019, we owned two issued U.S. patents, which are not due to expire before 2035, excluding any additional term for patent term adjustment or extension; two pending U.S. patent applications, which, if issued, are not due to expire before 2035 and 2036, respectively, excluding any additional term for patent term adjustment or extension; and a number of patent applications in other jurisdictions. As of December 31, 2019, we jointly owned, with University of Michigan, three issued U.S. patents, which are each not due to expire before 2033, excluding any additional term for patent term adjustments or extensions; one pending U.S. patent application, which, if issued, is not due to expire before 2033, excluding any additional term for patent term adjustment or extension; and a number of patent applications in other jurisdictions. The foregoing patents and patent applications cover a form of and methods of making and using nevanimibe or its analogs. Related international patent applications have issued in Australia, China, Japan, Mexico, and New Zealand and are pending in a number of other countries, including Australia, Brazil, Canada, China, Europe, and Mexico.

MLE-301

With respect to MLE-301 patent rights, as of December 31, 2019, we owned one pending U.S. patent application, which, if issued, is not due to expire before 2040, excluding any additional term for patent term adjustment or extension. As of December 31, 2019, we exclusively licensed from Roche one issued U.S. patent, which is not due to expire before 2031, excluding any additional term for patent term adjustment or extension. The foregoing patents and patent applications cover a form of and methods of making and using MLE-301 or its analogs. Related international patent applications have issued in China, Europe, Japan, South Korea, and Mexico, and are pending in a number of other countries, including Brazil, Canada, India, and Russia.

Manufacturing

We rely on contract manufacturing organizations, or CMOs, to produce drug candidates in accordance with the FDA's current Good Manufacturing Practices, or cGMP, regulations for use in our clinical trials. The manufacture of pharmaceuticals is subject to extensive cGMP regulations, which impose various procedural and documentation requirements and govern all areas of record keeping, production processes and controls, personnel and quality control. Our peptide and small molecule drug candidates (livoletide, nevanimibe and MLE-301) are manufactured using common chemical engineering and synthetic processes from readily available raw materials.

To meet our projected needs for clinical supplies to support its activities through regulatory approval and commercial manufacturing, the CMOs with whom we currently work may need to increase the scale of production or we will need to secure alternate suppliers. We believe that there are multiple potential sources for our contract manufacturing, but we have not engaged alternate suppliers in the event that our current CMOs are unable to scale production. Our relationships with CMOs are managed by internal personnel with extensive experience in pharmaceutical development and manufacturing.

If we are unable to obtain sufficient quantities of drug candidates or receive raw materials in a timely manner, we could be required to delay our ongoing clinical trials and seek alternative manufacturers, which would be costly and time-consuming.

Government Regulation and Approval

United States-FDA process

In the United States, the FDA regulates drugs. The Federal Food, Drug, and Cosmetic Act, or FDCA, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of drugs. To obtain regulatory approvals in the United States and in foreign countries, and subsequently comply with applicable statutes and regulations, we will need to spend substantial time and financial resources.

Approval process

The FDA must approve any new drug or a drug with certain changes to a previously approved drug before a manufacturer can market it in the United States. If a company does not comply with applicable United States requirements it may be subject to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending applications, warning or untitled letters, clinical holds, drug recalls, drug seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution. The steps we must complete before we can market a drug include:

- completion of preclinical laboratory tests, animal studies, and formulation studies, all performed in accordance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical studies start. The sponsor must update the IND annually;
- approval of the study by an independent institutional review board, or IRB, or ethics committee representing each clinical site before each clinical study begins;
- performance of adequate and well-controlled human clinical studies to establish the safety and efficacy of the drug for each indication to the FDA's satisfaction;
- submission to the FDA of an NDA;

- potential review of the drug application by an FDA advisory committee, where appropriate and if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities to assess compliance with current good manufacturing practices, cGMP, or regulations; and
- FDA review and approval of the NDA.

It generally takes companies many years to satisfy the FDA approval requirements, but this varies substantially based upon the type, complexity, and novelty of the drug or disease. Preclinical tests include laboratory evaluation of a drug's chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the drug. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLP. The company submits the results of the preclinical testing to the FDA as part of an IND along with other information, including information about the product drug's chemistry, manufacturing and controls, and a proposed clinical study protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, are generally conducted after submitting the initial IND.

The FDA requires a 30-day waiting period after the submission of each IND before the company can begin clinical testing in humans in the United States. The FDA may, within the 30-day time period, raise concerns or questions relating to one or more proposed clinical studies and place the study on a clinical hold. In such a case, the company and the FDA must resolve any outstanding concerns before the company begins the clinical study. Accordingly, the content of an IND submission may or may not be sufficient for the FDA to permit the sponsor to start a clinical study. The company must also make a separate submission to an existing IND for each successive clinical study conducted in the U.S. during drug development.

Clinical studies

Clinical studies involve administering the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. The company must conduct clinical studies:

- in compliance with federal regulations;
- in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical study sponsors, administrators, and monitors; as well as
- under protocols detailing the objectives of the trial, the safety monitoring parameters, and the effectiveness criteria.

The company must submit each protocol involving testing on United States patients and subsequent protocol amendments to the FDA as part of the IND. The FDA may order the temporary, or permanent, discontinuation of a clinical study at any time, or impose other sanctions, if it believes that the sponsor is not conducting the clinical study in accordance with FDA requirements or presents an unacceptable risk to the clinical study patients. The sponsor must also submit the study protocol and informed consent information for patients in clinical studies to an institutional review board for approval. An IRB may halt the clinical study, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Companies generally divide the clinical investigation of a drug into three or four phases. While companies usually conduct these phases sequentially, they are sometimes overlapped or combined.

- *Phase 1.* The company evaluates the drug in healthy human subjects or patients with the target disease or condition. These studies typically evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational new drug in humans, the side effects associated with increasing doses, and if possible, gain early evidence on effectiveness.
- *Phase 2.* The company administers the drug to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks, and preliminarily evaluate efficacy.
- *Phase 3.* The company administers the drug to an expanded patient population, generally at geographically dispersed clinical study sites, to generate enough data to statistically evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug, and to provide an adequate basis for product approval.
- *Phase 4.* In some cases, the FDA may condition approval of an NDA for a drug on the company's agreement to conduct additional clinical studies after approval. In other cases, a sponsor may voluntarily conduct additional

clinical studies after approval to gain more information about the drug. We typically refer to such post-approval studies as Phase 4 clinical studies.

A pivotal study is a clinical study that adequately meets regulatory agency requirements to evaluate a drug's efficacy and safety to justify the approval of the drug. Generally, pivotal studies are Phase 3 studies, but the FDA may accept results from Phase 2 studies if the study design provides a well controlled and reliable assessment of clinical benefit, particularly in situations in which there is an unmet medical need and the results are sufficiently robust.

The FDA, the IRB, or the clinical study sponsor may suspend or terminate a clinical study at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Additionally, an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or committee, may oversee some clinical studies. This group provides authorization for whether or not a study may move forward at designated checkpoints based on access to certain data from the study. We may also suspend or terminate a clinical study based on evolving business objectives and the competitive climate.

Submission of an NDA

After a company completes the required clinical testing, it can prepare and submit an NDA to the FDA, who must approve the NDA before it can start marketing the drug in the United States. An NDA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the drug's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical studies on a drug, or from a number of alternative sources, including studies initiated by investigators or studies not conducted under a U.S. IND. To support marketing authorization, the data we submit must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug to the FDA's satisfaction.

The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, and the manufacturer and/or sponsor under an approved new drug application are also subject to annual program user fees. The FDA typically increases these fees annually. Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers.

The FDA has 60 days from its receipt of an NDA to determine whether it will accept the application for filing based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. Once the FDA accepts the filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Under the Prescription Drug User Fee Act, the FDA has a goal of responding to standard review NDAs within ten months after the 60-day filing review period, but this timeframe may be extended. The FDA reviews most applications for standard review drugs within ten to 12 months and most applications for priority review drugs within six to eight months. Priority review can be applied to drugs that the FDA determines offer major advances in treatment, or provide a treatment where no adequate therapy exists.

The FDA may also refer applications for novel drugs that present difficult questions of safety or efficacy, to an advisory committee. This is typically a panel that includes clinicians and other experts that will review, evaluate, and recommend whether the FDA should approve the application. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP, and will inspect the facility or the facilities at which the drug is manufactured. The FDA will not approve the drug unless compliance with cGMP is satisfactory and the NDA contains data that provide evidence that the drug is safe and effective in the indication studied.

The FDA's decision on an NDA

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter indicates that the FDA has completed its review of the application, and the agency has determined that it will not approve the application in its present form. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional clinical data and/or other significant, expensive, and time-consuming requirements related to clinical studies, preclinical studies and/or manufacturing. The FDA has committed to reviewing resubmissions of the NDA addressing such deficiencies in two or six months, depending on the type of information included. Even if we submit such data, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Also, the government may establish additional requirements, including those resulting from new legislation, or the FDA's policies may change, which could delay or prevent regulatory approval of our drugs under development.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include communication plans for healthcare professionals, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for REMS can materially affect the potential market and profitability of the drug. Moreover, the FDA may condition approval on substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, the FDA may withdraw drug approvals if the company fails to comply with regulatory standards or identifies problems following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before we can implement the change. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing new NDAs. As with new NDAs, the FDA often significantly extends the review process with requests for additional information or clarification.

Post-approval requirements

The FDA regulates drugs that are manufactured or distributed pursuant to FDA approvals and has specific requirements pertaining to recordkeeping, periodic reporting, drug sampling and distribution, advertising and promotion and reporting of adverse experiences with the drug. After approval, the FDA must provide review and approval for most changes to the approved drug, such as adding new indications or other labeling claims. There also are continuing, annual user fee requirements for any marketed drugs and the establishments who manufacture its drugs, as well as new application fees for supplemental applications with clinical data.

Drug manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. There are strict regulations regarding changes to the manufacturing process, and, depending on the significance of the change, it may require prior FDA approval before we can implement it. 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 area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if a company does not comply with regulatory requirements and maintain standards or if problems occur after the drug reaches the market. If a company or the FDA discovers previously unknown problems with a drug, including adverse events of unanticipated severity or frequency, issues with manufacturing processes, or the company's failure to comply with regulatory requirements, the FDA may revise the approved labeling to add new safety information; impose post-marketing studies or other clinical studies to assess new safety risks; or impose distribution or other restrictions under a REMS program. Other potential consequences may include:

- restrictions on the marketing or manufacturing of the drug, complete withdrawal of the drug from the market or drug recalls;
- fines, warning letters or holds on post-approval clinical studies;
- the FDA refusing to approve pending NDAs or supplements to approved NDAs, or suspending or revoking of drug license approvals;
- drug seizure or detention, or refusal to permit the import or export of drugs; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of drugs that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is otherwise consistent with the product's FDA approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. We could be subject to significant liability if we violated these laws and regulations.

Marketing Exclusivity

In addition to patent term (as extended by the Hatch-Waxman Act), the holder of the NDA for a listed drug may be entitled to a period of marketing exclusivity, during which the FDA cannot approve an abbreviated new drug application, or ANDA, or 505(b)(2) application that relies on the listed drug. For example, a pharmaceutical manufacturer may obtain five years of non-patent exclusivity upon NDA approval of a new chemical entity, or NCE, which is a drug that contains an active moiety that has not been approved by FDA in any other NDA. An "active moiety" is defined as the molecule or ion responsible for the drug substance's physiological or pharmacological action. During the five year exclusivity period, the FDA cannot accept for filing any ANDA seeking approval of a generic version of that drug or any 505(b)(2) NDA for the same active moiety and that relies on the FDA's findings regarding that drug, except that FDA may accept an application for filing after four years if the follow-on applicant makes a paragraph IV certification.

A drug, including one approved under Section 505(b)(2), may obtain a three-year period of exclusivity for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical studies (other than bioavailability or bioequivalence studies) was essential to the approval of the application and was conducted/sponsored by the applicant. Should this occur, the FDA would be precluded from approving any ANDA or 505(b)(2) application for the protected modification until after that three-year exclusivity period has run. However, unlike NCE exclusivity, the FDA can accept an application and begin the review process during the exclusivity period.

Orphan drug designation

The FDA may grant orphan drug designation to sponsors of drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. In addition, if a drug receives FDA approval for the indication for which it has orphan designation, the drug may be entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the drug with orphan exclusivity.

Pediatric information

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which the FDA has granted an orphan designation.

Healthcare reform

In the United States and foreign jurisdictions, the legislative landscape continues to evolve. There have been a number of legislative and regulatory changes to the healthcare system that could affect the future results of our operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reform the way in which healthcare is funded and reduce healthcare costs. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively PPACA, was enacted, which included measures that have significantly changed health care financing by both governmental and private insurers. The provisions of PPACA of importance to the pharmaceutical and biotechnology industry are, among others, the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- expansion of healthcare fraud and abuse laws, including the federal civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians, as defined by such law, and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members; and
- new requirement to annually report certain drug samples that manufacturers and distributors provide to licensed practitioners, or to pharmacies of hospitals or other healthcare entities.

There remain judicial and Congressional challenges to certain aspects of the PPACA, as well as efforts by the Trump administration to repeal or replace certain aspects of the PPACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the PPACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or Tax Act, included a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. The Bipartisan Budget Act of 2018, among other things, amended the PPACA to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". In December 2018, the Centers for Medicare & Medicaid Services, or CMS, published a new final rule permitting further collections and payments to and from certain PPACA qualified health plans and health insurance issuers under the PPACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the PPACA will impact the PPACA.

In addition, other health reform measures have been proposed and adopted in the United States since PPACA was enacted. For example, as a result of the Budget Control Act of 2011, as amended, providers are subject to Medicare payment reductions of 2% per fiscal year through 2029 unless additional Congressional action is taken. Further, the American Taxpayer Relief Act of 2012 reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments from providers from three to five years.

More recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Further, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and has

implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. While some measures may require additional authorization to become effective, 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, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

European Union-EMA process

In the European Union, our product candidates are also be subject to extensive regulatory requirements. As in the United States, medicinal products can only be marketed if a marketing authorization, or MA, from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Clinical trials of medicinal products in the European Union must be conducted in accordance with European Union and national regulations and the International Conference on Harmonization, or ICH, guidelines on Good Clinical Practices, or GCP. Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the European Union clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. To improve the current system, Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, which repealed Directive 2001/20/EC, was adopted on April 16, 2014 and published in the European Official Journal on May 27, 2014. The Regulation aims to harmonize and streamline the clinical trials authorization process, simplify adverse event reporting procedures, improve the supervision of clinical trials, and increase their transparency. Although the Regulation entered into force on June 16, 2014, it will not be applicable until six months after the full functionality of the IT portal and database envisaged in the Regulation is confirmed by an independent audit, and the European Commission publishes a notice of this confirmation. This is not expected to occur until before 2021 as an audit of the system is intended to commence in December 2020. Until then the Clinical Trials Directive 2001/20/EC will still apply.

In addition, the transitory provisions of the new Regulation offer the sponsors the possibility to choose between the requirements of the Directive and the Regulation for one year from the entry into application of the Regulation.

Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU Member States where the trial is to be conducted by two distinct bodies: the National Competent Authority, or NCA, and one or more Ethics Committees, or ECs. Under the current regime all suspected unexpected serious adverse reactions, or SUSARs, to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred and would also be reported in all countries where the drug is being used in a clinical trial.

Approval Process

Under the centralized procedure, after the EMA issues an opinion, the European Commission issues a single marketing authorization valid across the European Union, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for human drugs that are: derived from biotechnology processes, such as genetic engineering; contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders diseases or autoimmune diseases and other immune dysfunctions; advanced-therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines; and officially designated orphan drugs. For drugs that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMA, as long as the drug concerned contains a new active substance; is a significant therapeutic, scientific or technical innovation; or if its authorization would be in the interest of public health.

There are also three other possible routes to authorize medicinal products in the European Union, which are available for products that fall outside the scope of the centralized procedure:

- National procedure. National MAs, issued by the competent authorities of the Member States of the EEA, are available however these only cover their respective territory;

- Decentralized procedure. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of a medicinal product that has not yet been authorized in any European Union country; and

- Mutual recognition procedure. In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Thereafter, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

We do not foresee that livoletide for the treatment of hyperphagia in patients with PWS and nevanimibe for the treatment of CAH will be suitable for a National MA as they fall within the mandatory criteria for the centralized procedure. Therefore, these product candidates will be reviewed and approved through centralized procedure. MLE-301 for the treatment of VMS does not fall within the mandatory criteria for the centralized procedure. We may request review and approval through the centralized procedure for this product candidate, or we may seek review and approval through the mutual recognition procedure.

Pursuant to Regulation (EC) No 1901/2006, all applications for marketing authorization for new medicines must include the results of all studies performed and details of all information collected in compliance with as described in a pediatric investigation plan, or PIP, agreed between regulatory authorities, the EMA's Pediatric Committee, and the applicant, unless the medicine is exempt because of a deferral or waiver (e.g., because the relevant disease or condition occurs only in adults). Applicants are encouraged to submit pediatric investigation plans early during product development, in time for studies to be conducted in the pediatric population, where appropriate, before marketing authorization applications are submitted. Before the EMA is able to begin its assessment of a centralized procedure MA application, it will validate that the applicant has complied with an agreed pediatric investigation plan, or an application for a waiver has been submitted. The applicant and the EMA may, where such a step is adequately justified, agree to modify a pediatric investigation plan to assist validation. Modifications are not always possible; may take longer to agree than the period of validation permits; and may still require the applicant to withdraw its marketing authorization application, or MA, and to conduct additional non-clinical and clinical studies. Products that are granted a MA on the basis of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate or a patent qualifying for a supplementary protection (if any is in effect at the time of approval) or certificate or, in the case of orphan medicinal products, a two year extension of the orphan market exclusivity. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Orphan drug designation

In the European Union, Regulation (EC) No 141/2000, as amended, states that a drug will be designated as an orphan drug if its sponsor can establish:

- that it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or that it is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the drug in the European Union would generate sufficient return to justify the necessary investment; and

- that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Union or, if such method exists, that the drug will be of significant benefit to those affected by that condition.

Regulation (EC) No 847/2000 sets out further provisions for implementation of the criteria for designation of a drug as an orphan drug. An application for the designation of a drug as an orphan drug may be submitted at any stage of development of the drug before submission of a MA application. However, an application for designation as an orphan drug may be submitted for a new therapeutic indication for an already authorized medicinal product.

If a centralized procedure MA in respect of an orphan drug is granted pursuant to Regulation (EC) No 726/2004, regulatory authorities will not, for a period of 10 years, accept another application for a MA, or grant a MA or accept an application to extend an existing MA, for the same therapeutic indication, in respect of a similar drug. This period may however be reduced to six years if, at the end of the fifth year, it is established, in respect of the drug concerned, that the criteria for orphan drug designation are no longer met, for example, when it is shown on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity. The exclusivity period may increase to 12 years if, among other

things, the MA includes the results of studies from an agreed pediatric investigation plan. Notwithstanding the foregoing, a MA may be granted for the same therapeutic indication to a similar drug if:

- the holder of the MA for the original orphan drug has given its consent to the second applicant;
- the holder of the MA for the original orphan drug is unable to supply sufficient quantities of the drug; or
- the second applicant can establish in the application that the second drug, although similar to the orphan drug already authorized, is safer, more effective or otherwise clinically superior.

Regulation (EC) No 847/2000 lays down definitions of the concepts 'similar drug' and 'clinical superiority'. Other incentives available to orphan drugs in the European Union include financial incentives such as a reduction of fees or fee waivers and protocol assistance. Orphan drug designation does not shorten the duration of the regulatory review and approval process.

Good manufacturing practices

Like the FDA, the EMA, the competent authorities of the European Union Member States and other regulatory agencies regulate and inspect equipment, facilities and processes used in the manufacturing of drugs intended for the EU market to ensure that certain minimum standards are met. These requirements apply, no matter where in the world the manufacturing process takes place and are designed to ensure that products intended for the EU market are of consistent high quality, are appropriate for their intended use and meet the requirements of the marketing authorization or clinical trial authorization. If, after receiving clearance from regulatory agencies, a company makes a material change in manufacturing equipment, location, or process, additional regulatory review and approval may be required. We and our partners will be required to continue to comply with cGMP, and drug-specific regulations enforced by, the European Commission, the EMA and the competent authorities of European Union Member States following drug approval. Also like the FDA, the EMA, the competent authorities of the European Union Member States and other regulatory agencies also conduct regular, periodic visits to reinspect equipment, facilities, and processes following the initial approval of a drug. If, as a result of these inspections, the regulatory agencies determine that we or our partners' equipment, facilities, or processes do not comply with applicable regulations and conditions of drug approval, they may seek civil, criminal or administrative sanctions and/or remedies against us, including the suspension of its manufacturing operations or the withdrawal of our drug from the market.

Post-Approval Controls

The holder of a European MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance, or QPPV, who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports, or PSURs.

All new MAs must include a risk management plan, or RMP, describing the risk management system that the company will put in place, recording the product's safety profile and documenting the effectiveness of risk-minimization measures. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies. RMPs and PSURs are routinely available to third parties requesting access, subject to limited redactions. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off-label promotion is prohibited. Direct-to-consumer advertising of prescription medicines is also prohibited in the European Union. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each EU Member State and can differ from one country to another.

Data and market exclusivity

Similar to the United States, there is a process to authorize generic versions of innovative drugs in the European Union. Generic competitors can, where data exclusivity has expired, submit abridged applications to authorize generic versions of drugs authorized by the EMA through the centralized procedure referencing the innovator's data and demonstrating bioequivalence to the reference drug, among other things. If a marketing authorization is granted for a medicinal product containing a new active substance, that product benefits from eight years of data exclusivity, during which generic marketing authorization applications referring to the data of that product may not be accepted by the regulatory authorities, and a further two years of market exclusivity, during which such generic products may not be placed on the market. The two-year period may be extended to three years if during the first eight years a new therapeutic indication with significant clinical benefit over existing therapies is approved. This system is usually referred to as "8+2". There is also a special regime for biosimilars, or biological medicinal

products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example, because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. In addition, there are certain circumstances, such as where the innovator company is granted a marketing authorization for a significant new indication for the relevant medicinal product, where an additional one year of marketing exclusivity may be granted. As referenced above, orphan medicinal products are subject to separate marketing exclusivity arrangements.

Other international markets-drug approval process

In some international markets (such as China or Japan), although data generated in United States or European Union trials may be submitted in support of a marketing authorization application, regulators may require additional clinical studies conducted in the host territory, or studying people of the ethnicity of the host territory, prior to the filing or approval of marketing applications within the country.

Pricing and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drugs for which we may obtain regulatory approval. In the United States and markets in other countries, sales of any drugs for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care plans, private health insurers and other organizations. The process for determining whether a third-party payor will provide coverage for a drug may be separate from the process for setting the reimbursement rate that the payor will pay for the drug. Third-party payors may limit coverage to specific drugs on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Moreover, a third-party payor's decision to provide coverage for a drug does not imply that an adequate reimbursement rate will be approved. Additionally, coverage and reimbursement for drugs can differ significantly from payor to payor. One third-party payor's decision to cover a particular drug does not ensure that other payors will also provide coverage for the drug, or will provide coverage at an adequate reimbursement rate. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on its investment in drug development.

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

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 health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic drugs for branded prescription drugs. By way of example, PPACA contains provisions that may reduce the profitability of drugs, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for our drugs.

In the European Community, governments influence the price of drugs through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those drugs to consumers. Some jurisdictions operate positive and negative list systems under which drugs may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical studies that compare the cost effectiveness of a particular drug candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new drugs. In addition, in some countries, cross border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any drugs for which we receive regulatory approval for commercial sale may suffer if government and other third-party payors fail to provide coverage and adequate reimbursement. In addition, the focus on cost containment

measures in the United States and other countries has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time.

Other healthcare laws impacting sales, marketing, and other company activities

Numerous regulatory authorities in addition to the FDA, including, in the United States, CMS, other divisions of the U.S. Department of Health and Human Services, or HHS, the U.S. Department of Justice, and similar foreign, state, and local government authorities, regulate and enforce laws and regulations applicable to sales, promotion and other activities of pharmaceutical manufacturers. These laws and regulations may impact, among other things, our clinical research programs, proposed sales and marketing and education activities, and financial and business relationships with future prescribers of our product candidates, once approved. These laws and regulations include U.S. federal, U.S. state and foreign anti-kickback, false claims, and data privacy and security laws, which are described below, among other legal requirements that may affect our current and future operations.

The FDA regulates all advertising and promotion activities for drugs under its jurisdiction both prior to and after approval. Only those claims relating to safety and efficacy that the FDA has approved may be used in labeling once the drug is approved. Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those we tested and the FDA approved. Such off-label uses are common across medical specialties, and often reflect a physician's belief that the off-label use is the best treatment for the patients. The FDA does not regulate the behavior of physicians in their choice of treatments, but FDA regulations do impose stringent restrictions on manufacturers' communications regarding off-label uses. If we do not comply with applicable FDA requirements we may face adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA. Promotion of off-label uses of drugs can also implicate the false claims laws described below.

Anti-kickback laws including, without limitation, the federal Anti-Kickback Statute that applies to items and services reimbursable under governmental healthcare programs such as Medicare and Medicaid, make it illegal for a person or entity to, among other things, knowingly and willfully solicit, receive, offer or pay remuneration, directly or indirectly, to induce, or in return for, purchasing, leasing, ordering, or arranging for or recommending the purchase, lease, or order of any good, facility, item, or service reimbursable, in whole or in part, under a federal healthcare program. Due to the breadth of the statutory provisions and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that our practices might be challenged under anti-kickback or similar laws. Moreover, recent healthcare reform legislation has strengthened these laws. For example, PPACA among other things, amends the intent requirement of the federal Anti-Kickback Statute and certain other criminal healthcare fraud statutes to clarify that a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a crime. In addition, PPACA clarifies that the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

False claims laws, including, without limitation, the federal civil False Claims Act, and civil monetary penalty laws prohibit, among other things, anyone from knowingly and willingly presenting, or causing to be presented for payment, to the federal government (including Medicare and Medicaid) claims for reimbursement for, among other things, drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Our activities relating to the sales and marketing of its drugs may be subject to scrutiny under these laws, as well as civil monetary penalties laws and the criminal healthcare fraud provisions enacted as part of the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA.

HIPAA imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or 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. Similar to the U.S. federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations governs the conduct of certain electronic healthcare transactions and imposes requirements with respect to safeguarding the security and privacy of protected health information on HIPAA covered entities and their business associates who provide services involving HIPAA protected health information to such covered entities.

The federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS information related to payments or other "transfers of value" made to physicians

(defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members.

In addition, we may be subject to state law equivalents of each of the above federal laws, such as anti-kickback, self-referral, and false claims laws which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical manufacturers to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers; state laws that require pharmaceutical manufacturers to file reports with states regarding marketing information, such as the tracking and reporting of gifts, compensation and other remuneration and items of value provided to healthcare professionals and entities; state laws that require the reporting of information related to drug pricing; state and local laws requiring the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of personal data and protected health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

Violations of these laws may result in significant criminal, civil and administrative sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid), disgorgement, contractual damages, reputational harm and the imposition of corporate integrity agreements or other similar agreements with governmental entities, which may impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties, as well as imprisonment, also can be imposed upon executive officers and employees, including criminal sanctions against executive officers under the so-called "responsible corporate officer" doctrine, even in situations where the executive officer did not intend to violate the law and was unaware of any wrongdoing. Given the significant penalties and fines that can be imposed on companies and individuals if convicted, allegations of such violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions and additional corporate integrity obligations. If the government were to allege or convict us or our executive officers of violating these laws, our business could be harmed.

Similar rigorous restrictions are imposed on the promotion and marketing of drugs in the European Union and other countries. Even in those countries where we may not be directly responsible for the promotion and marketing of our drugs, if our potential international distribution partners engage in inappropriate activity it can have adverse implications for us.

Employees

As of March 1, 2020, we had 38 employees, 37 of whom were full-time employees and 1 of whom was a part-time employee. As of March 1, 2020, 18 of our employees were engaged in research and development activities and 20 of our employees were engaged in business development, commercial, finance, information systems, facilities, human resources or administrative support. As of March 1, 2020, we had 35 employees located in the United States and 3 employees located in France. None of our U.S. employees are represented by any collective bargaining agreements. Our French employees are represented by a collective bargaining agreement. We believe that we maintain good relations with our employees.

Merger

On December 7, 2018, OvaScience, Inc., or OvaScience, now known as Millendo Therapeutics, Inc., completed its reverse merger or, the Merger, with what was then known as "Millendo Therapeutics, Inc.," or Private Millendo, in accordance with the terms of the Agreement and Plan of Merger and Reorganization dated as of August 8, 2018, as amended on September 25, 2018 and November 1, 2018. OvaScience's shares of common stock listed on The Nasdaq Capital Market, previously trading through the close of business on Friday, December 7, 2018 under the ticker symbol "OVAS," commenced trading on The Nasdaq Capital Market, under the ticker symbol "MLND," on Monday, December 10, 2018.

Immediately following the Merger, Private Millendo became a wholly-owned subsidiary of OvaScience. Upon consummation of the Merger, OvaScience adopted the business plan of Private Millendo and discontinued the pursuit of OvaScience's business plan pre-Closing.

Available Information

Our internet website address is www.millendo.com. In addition to the information about us and our subsidiaries contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission, or SEC. Additionally the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC's website is www.sec.gov.

ITEM 1A. RISK FACTORS

You should carefully consider the risks described below, as well as general economic and business risks and the other information in this Annual Report on Form 10-K. The occurrence of any of the events or circumstances described below or other adverse events could have a material adverse effect on our business, results of operations and financial condition and could cause the trading price of our common stock to decline. Additional risks or uncertainties not presently known to us or that we currently deem immaterial may also harm our business.

Risks Related to the Merger

The risks arising with respect to the historic OvaScience business and operations may be different from what we anticipate, which could lead to significant, unexpected costs and liabilities and could materially and adversely affect our business going forward.

It is possible that we may not have fully anticipated the extent of the risks associated with the Merger we completed with OvaScience in 2018. After the Merger, OvaScience's historic business was discontinued, but prior to the transaction OvaScience had a significant operating history. As a consequence, we may be subject to claims, demands for payment, regulatory issues, costs and liabilities that were not and are not currently expected or anticipated. Notwithstanding our exercise of due diligence pre-transaction and winding down of the OvaScience business post-transaction, the risks involved with taking over a business with a significant operating history and the costs and liabilities associated with these risks may be greater than we anticipate. We may not be able to contain or control the costs or liabilities associated with OvaScience's historic business, which could materially and adversely affect our business, liquidity, capital resources or results of operation.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant operating losses since inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses and negative operating cash flows and there is no assurance that we will ever achieve or sustain profitability. Our net loss was $27.2 million and $44.6 million for the years ended December 31, 2018 and 2019, respectively. As of December 31, 2019, we had an accumulated deficit of $208.7 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We have devoted substantially all of our efforts to the acquisition of and preclinical and clinical development of two of our product candidates, livoletide and nevanimibe, as well as to building our management team and infrastructure. It could be several years, if ever, before we have a commercialized product and our commercialized products, if any, may not be profitable. The net losses we incur may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase significantly in connection with our ongoing activities such as:

- continuing the ongoing and planned clinical development of livoletide and nevanimibe;
- continuing the preclinical development and potential clinical development of MLE-301;
- initiating preclinical studies and clinical trials for any additional diseases for our current product candidates and any future product candidates that we may pursue;
- building a portfolio of product candidates through the acquisition or in-license of drugs or product candidates and technologies;
- developing, maintaining, expanding and protecting our intellectual property portfolio;
- manufacturing, or having manufactured, clinical and commercial supplies of our product candidates;
- seeking marketing approvals for our current and future product candidates that successfully complete clinical trials;

- establishing a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- hiring additional administrative, clinical, regulatory and scientific personnel; and
- continuing to incur additional costs associated with operating as a public company.

In order to become and remain profitable, we will need to develop and eventually commercialize, on our own or with collaborators, one or more product candidates with significant market potential. This will require us to be successful in a range of challenging activities, including completing clinical trials of livoletide, nevanimibe, and MLE-301, developing commercial scale manufacturing processes, obtaining marketing approval, manufacturing, marketing and selling any current and future product candidates for which we may obtain marketing approval, and satisfying any post-marketing requirements. We may never succeed in any or all of these activities and, even if we do, we may never generate revenue from product sales or achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical products and development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the U.S. Food and Drug Administration (the "FDA") or other regulatory authorities such as the European Medicines Agency (the "EMA") to amend existing studies or trials, to perform studies and trials in addition to those currently expected, or if there are any delays in the development or in the completion of any planned or future preclinical studies or clinical trials of our current or future product candidates, our expenses could increase and profitability could be further delayed. For example, and as previously disclosed in our periodic reports in 2019, enrollment for our Phase 2b CAH clinical trial was previously paused in certain countries while appropriate regulatory authorities and ethics committees reviewed our submissions for a protocol amendment.

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 decrease our value and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in our value also could cause you to lose all or part of your investment.

We have a limited operating history and have never generated any revenue from product sales, which may make it difficult to assess our future viability.

We are a clinical stage biopharmaceutical company with a limited operating history. Our operations to date, with respect to the development of our product candidates, have been limited to organizing and staffing the business, business planning, raising capital, acquiring our product candidates and other assets and conducting preclinical and clinical development of our product candidates. We have not yet demonstrated an ability to successfully complete clinical development of a product candidate, obtain marketing approval, manufacture a commercial-scale drug (or arrange for a third-party to do so on our behalf), or conduct sales and marketing activities necessary for successful commercialization. Consequently, our predictions about our future success or viability may not be as accurate as they could be if we had more experience developing product candidates.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with any future collaborations, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, livoletide, nevanimibe and any additional product candidates that we may pursue in the future. We do not anticipate generating revenue from product sales for the next several years, if ever. Our ability to generate revenue from product sales depends heavily on our or any future collaborators' success in:

- timely and successful completion of development activities of our current product candidates;
- obtaining and maintaining regulatory and marketing approvals for livoletide, nevanimibe and any future product candidates for which we successfully complete clinical trials;
- launching and commercializing any product candidates for which we obtain regulatory and marketing approval by establishing a sales force, marketing and distribution infrastructure or, alternatively, collaborating with a commercialization partner;
- qualifying for coverage and adequate reimbursement by government and third-party payors for our current or any future product candidates, if approved, both in the United States and internationally, and reaching acceptable agreements with such government and third-party payors on pricing terms;

- developing, validating and maintaining a commercially viable, sustainable, scalable, reproducible and transferable manufacturing process for livoletide, nevanimibe or any future product candidates that are compliant with current good manufacturing practices, or cGMP;
- establishing and maintaining supply and manufacturing relationships with third-parties that can provide an adequate amount and quality of drugs and services to support our planned clinical development, as well as the market demand for livoletide, nevanimibe and any future product candidates, if approved;
- obtaining market acceptance, if and when approved, of livoletide, nevanimibe or any future product candidates as a viable treatment option by physicians, patients, third-party payors and others in the medical community;
- effectively addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter, and performing our obligations pursuant to such arrangements;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how;
- avoiding and defending against third-party interference or infringement claims; and
- attracting, hiring and retaining qualified personnel.

We will require additional capital to finance our operations, which may not be available on acceptable terms, if at all. Failure to obtain capital when needed may force us to delay, limit or terminate certain of our development programs, future commercialization efforts or other operations.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to develop, and if approved, commercialize, livoletide, nevanimibe, and MLE-301. Additionally, if we obtain marketing approval for our product candidates, we expect to incur significant expenses related to manufacturing, marketing, sales and distribution. Furthermore, we expect to continue to incur additional costs associated with operating as a public company.

As of December 31, 2019, our cash, cash equivalents, marketable securities and restricted cash were $63.5 million. Our existing cash, cash equivalents, marketable securities and restricted cash, in addition to estimated net proceeds of approximately $5.5 million received in March 2020, in connection with shares issued under the ATM equity distribution agreement, are currently expected to be sufficient to fund our current operating plans into 2022. However, this cash runway guidance is based on our current operational plans and excludes any additional funding that may be received and business development or commercialization activities that may be undertaken. In addition, our operating plans may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, third-party funding, and marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. In any event, we will require additional capital to pursue preclinical and clinical activities, regulatory approval and the commercialization of our current and future product candidates. Even if we believe we have sufficient capital for our current operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations. If we elect to do so, additional capital may not be available to us on acceptable terms, if at all. Our ability to access additional capital, and as a result our operating results and liquidity needs, could be negatively affected by market fluctuations and economic downturn. Any additional capital raising efforts may divert our management from its day-to-day activities, which may adversely affect our ability to develop and commercialize our current and future product candidates.

Raising additional capital by issuing equity or debt securities may cause dilution to our existing stockholders, and raising funds through lending and licensing arrangements may restrict our operations or require us to relinquish proprietary rights.

Until such time as we can generate substantial revenue from product sales, if ever, we expect to finance our cash needs through a combination of equity and debt financings, strategic alliances and license and development agreements in connection with any future collaborations. To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership may experience substantial dilution, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. Equity and debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as redeeming our shares, making investments, incurring additional debt, making capital expenditures or declaring dividends.

The incurrence of indebtedness could result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants therein, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely affect our ability to conduct our business.

If we raise additional capital through collaborations, strategic alliances or third-party licensing arrangements, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional capital through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise develop and market ourselves.

We may be required to make payments under licenses applicable to livoletide, nevanimibe and MLE-301.

We have certain milestone and royalty payments related to livoletide, nevanimibe and MLE-301. We acquired worldwide, exclusive rights to nevanimibe pursuant to our license agreement with the Regents of the University of Michigan, or the University of Michigan, entered into in June 2013, or the UM License Agreement. Under the terms of the UM License Agreement, we are obligated to make significant milestone and royalty payments in connection with the attainment of certain development steps and the sale of resulting products with respect to nevanimibe, as well as other material obligations. In addition, pursuant to an assignment agreement for certain patents and patent applications relating to livoletide, we are also required to pay royalties on commercial sales and licensing of livoletide to the assignors. We acquired worldwide, exclusive rights to MLE-301 pursuant to a license agreement with F. Hoffmann-La Roche Ltd and Hoffman-La Roche Inc. (collectively, "Roche," and such agreement, the "Roche License Agreement"). Under the terms of the Roche License Agreement, we are obligated to make significant milestone and royalty payments in connection with the attainment of certain development steps and the sale of resulting products with respect to MLE-301, as well as other material obligations. In addition, we are required to share a portion of any net proceeds received in connection with certain agreements that we may enter into with third-parties to develop and commercialize MLE-301. If milestone or other non-royalty obligations become due, we may not have sufficient funds available to meet our obligations, which will materially adversely affect our business operations and financial condition. If milestone or other non-royalty obligations become due, we may not have sufficient funds available to meet our obligations, which will materially adversely affect our business operations and financial condition.

We may expend our limited resources to pursue a particular product candidate or disease and fail to capitalize on product candidates or diseases 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 respect to our own product candidates for additional indications and other product candidates or diseases that later prove to have greater commercial potential. Our resource allocation decisions may ultimately not result in successful clinical development programs and may cause us to fail to capitalize on other viable product candidates, commercial products or profitable market opportunities. In addition, our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. For example, and as previously disclosed, in our Phase 2 clinical trial for Cushing's syndrome ("CS"), we experienced slower than anticipated enrollment, which could have made impractical further development of nevanimibe for the treatment of CS. As a result of the difficulty in enrolling this trial, we elected to discontinue this Phase 2 clinical trial in August 2019 and have suspended development of nevanimibe for the treatment of CS.

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 sale, collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights.

Risks Related to Development and Commercialization

Our future success is dependent on the successful clinical development, regulatory approval and subsequent commercialization of livoletide, nevanimibe and any future product candidates. If we are not able to obtain the required regulatory approvals, we will not be able to commercialize our current or future product candidates and our ability to generate revenue will be adversely affected.

We do not have any drugs that have received regulatory approval and may never be able to develop marketable product candidates. We expect that a substantial portion of our efforts and expenses for the foreseeable future will be devoted to the clinical development of livoletide and nevanimibe, and as a result, our business currently depends heavily on the successful development, regulatory approval and commercialization of these product candidates. We cannot be certain that livoletide or

nevanimibe will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. The research, testing, manufacturing, safety, efficacy, labeling, approval, sale, marketing and distribution of our product candidates are, and will remain, subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and similar foreign regulatory authorities. Failure to obtain regulatory approval for livoletide or nevanimibe in the United States or other jurisdictions will prevent us from commercializing and marketing livoletide or nevanimibe.

The pivotal Phase 2b PWS trial, if persuasive statistically, may support the submission of an NDA in the United States or a marketing authorization application in Europe, for livoletide for the treatment of hyperphagia in patients with PWS. Additionally, the FDA may require additional data (for example, in younger children) in order to support an NDA approval in PWS in the United States.

Even if we were to successfully obtain approval from the FDA and comparable foreign regulatory authorities for our product candidates, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval for our product candidates, or any approval contains significant limitations, on our own or with any future collaborators, we may not be able to obtain sufficient funding or generate sufficient revenue to continue the development of any other product candidate that we may in-license, develop or acquire in the future.

Furthermore, even if we obtain regulatory approval for livoletide or nevanimibe, we will still need to develop a commercial infrastructure, or otherwise develop relationships with collaborators to commercialize, establish a commercially viable pricing structure and obtain approval for adequate reimbursement from third-party and government payors. If we, or our collaborators, are unable to successfully commercialize livoletide or nevanimibe, we may not be able to generate sufficient revenue to continue our business.

Preclinical studies or earlier clinical trials are not necessarily predictive of future results and the results of our clinical trials may not support our livoletide or nevanimibe claims.

Our orphan endocrine product candidates, livoletide and nevanimibe, are still in development and will require additional clinical testing before we are prepared to submit an NDA or other similar application for regulatory approval. We cannot predict with any certainty if or when we might submit an NDA for regulatory approval for livoletide or nevanimibe for the treatment of any indication or whether any such application will be approved by the relevant regulatory authority. Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. For instance, the FDA or foreign regulatory authorities may not agree with our proposed endpoints for any clinical trials of livoletide or nevanimibe, even if validated in prior clinical trials of similar product candidates, which may delay the commencement of our future clinical trials. The FDA or foreign regulatory authorities may also not agree with our proposed trial designs or dosing regimens, which may likewise prevent or delay the commencement of our future clinical trials. The clinical trial process is also time-consuming. We estimate that clinical trials of livoletide and nevanimibe for each of the indications that we are pursuing will take the next several years to complete. Failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon or repeat clinical trials. Further, we may encounter challenges in the clinical development of product candidates for reasons unrelated to the observed safety or efficacy of such product candidates in prior clinical trials. In addition, because we may at times pursue the treatment of multiple indications for a single product candidate, setbacks or failures in, or termination of, clinical development for one indication may have a negative impact on the clinical development for the treatment of other indications. For example, and as previously disclosed in our periodic reports in 2019, in our Phase 2 clinical trial for CS we have experienced slower than anticipated enrollment, which could have made impractical further development of nevanimibe for the treatment of CS. As a result of the difficulty in enrolling this trial, we elected to discontinue this Phase 2 clinical trial in August 2019 and have suspended development of nevanimibe for the treatment of CS.

Success in preclinical testing and early clinical trials does not ensure that later and pivotal clinical trials will generate the same results, or otherwise provide adequate data to demonstrate the safety and efficacy of a product candidate. Frequently, product candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later or pivotal clinical trials. For example, we expended substantial time and resources on a previous product candidate, MLE4901, an NK3R antagonist, which we ceased developing in 2017 due to concerns relating to elevated liver enzymes observed in clinical trials. Our approach to targeting orphan endocrine diseases where current therapies do not exist or are insufficient, is novel and unproven, and as such, the cost and time needed to develop livoletide and nevanimibe is difficult to predict and our efforts may not be successful. If we do not observe favorable results in future or planned clinical trials of livoletide and nevanimibe, we may decide to delay or abandon development of livoletide and nevanimibe, which could harm our business, financial condition and results of operations. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials.

We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of livoletide, nevanimibe and any future product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidate for its intended indications. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. For example, and as previously disclosed in our periodic reports in 2019, enrollment for our Phase 2b CAH clinical trial was previously paused in certain countries while appropriate regulatory authorities and ethics committees reviewed our submissions for a protocol amendment. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

- failure to obtain regulatory approval to commence a trial;
- unforeseen safety issues;
- determination of dosing issues;
- lack of effectiveness during clinical trials;
- inability to reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- slower than expected rates of patient recruitment, failure to recruit adequate numbers of suitable patients to participate in our clinical trials or failure to maintain participation of recruited patients in clinical trials;
- failure to manufacture sufficient quantities of a product candidate for use in clinical trials;
- inability to monitor patients adequately during or after treatment; and
- inability or unwillingness of medical investigators to follow our clinical protocols.

Further, we, the FDA, an institutional review board ("IRB"), or other regulatory authority may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including, for example, the FDA's good clinical practice ("GCP") regulations, that we are exposing participants to unacceptable health risks, or if the FDA or other regulatory authority, as the case may be, finds deficiencies in our investigational new drug ("IND"), application or other submissions, or the manner in which the clinical trials are conducted. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our current and future product candidates could be harmed, and our ability to generate revenue from our current or future product candidates, once approved, may be delayed or eliminated. In addition, any delays in our clinical trials could increase our costs, slow down the approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Moreover, principal investigators for our clinical trials may serve as our scientific advisors or consultants from time to time and receive compensation in connection with such services. We will be required to report these relationships to the FDA or other regulatory authorities as part of the drug approval process. The FDA or other regulatory authorities may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial results. They may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or other regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for our current product candidates or any future product candidates that we may develop.

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any NDAs that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. If the FDA does not accept or approve our NDAs for any of our product candidates, it may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of

these or any other FDA-required trials or studies, approval of any NDA or application that we submit may be delayed by several years, or may require us to expend more resources than it has available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability. If any of these outcomes occurs, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business, prospects, operating results and financial condition.

Enrollment and retention of patients in clinical trials is a competitive, expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.

Identifying and qualifying patients to participate in our clinical trials is critical to our success. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled we may be unable to retain a sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials, including our Phase 2b clinical trial of nevanimibe in patients with CAH, depends on many factors, including: the size of the patient population, the nature of the trial protocol, our ability to recruit clinical trial investigators with the appropriate competencies and experience, the existing body of safety and efficacy data with respect to the study drug, the number and nature of competing treatments and ongoing clinical trials of competing drugs for the same disease, the proximity of patients to clinical sites and the eligibility criteria for the trials, our ability to obtain and maintain patient consents and the risk that patients enrolled in clinical trials will drop out of the trials before completion.

The competitive nature of clinical trials in the pharmaceutical and biotechnology industries may make it difficult for us to recruit a sufficient number of patients to complete any of our clinical trials, or may increase costs. We may not be able to initiate or continue to support clinical trials of our product candidates for one or more indications, or any future product candidates, if we are unable to locate and enroll a sufficient number of eligible participants in these trials as required by the FDA or other regulatory authorities. For example, and as previously disclosed in our periodic reports in 2019, in our Phase 2 clinical trial for CS we have experienced slower than anticipated enrollment, which could have made impractical further development of nevanimibe for the treatment of CS. As a result of the difficulty in enrolling this trial, we elected to discontinue this Phase 2 clinical trial in August 2019 and have suspended development of nevanimibe for the treatment of CS. Even if we are able to enroll a sufficient number of patients in our clinical trials, if the pace of enrollment is slower than we expect, the development costs for our product candidates may increase and the completion of our trials may be delayed or our trials could become too expensive or impractical to complete.

Our ability to enroll and retain patients in clinical trials of livoletide may be adversely impacted by the fact that livoletide is administered by subcutaneous injection. Furthermore, any negative results we may report in clinical trials of our product candidates may make it difficult or impossible to recruit and retain patients in other clinical trials of those product candidates. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop livoletide and nevanimibe, or could render further development impossible. In addition, we may rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to compel their actual performance.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.

During the conduct of clinical trials, clinical investigators monitor changes in patients' health, including illnesses, injuries and discomforts. Often, it is not possible to determine whether or not the product candidate being investigated caused these conditions, and regulatory authorities may draw different conclusions or require additional testing to confirm these determinations if they occur. In addition, it is possible that as we test livoletide, nevanimibe or any other product candidate in larger, longer and more extensive clinical programs, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be observed or reported by subjects. If clinical testing indicates that livoletide, nevanimibe or any future product candidate has side effects or causes serious or life-threatening side effects, we may need to change the design of ongoing clinical trials or adjust dosing levels in ongoing or future clinical trials, and the development of the product candidate may be delayed or terminated entirely. For example, in recent years clinical trials by other companies evaluating product candidates for treatment of hyperphagia in patients with PWS, which employed a different mechanism of action than livoletide, have resulted in serious adverse events, including patient deaths, and the eventual termination of the clinical trial and/or clinical development program. Further, if the product candidate has received regulatory

approval, such approval may be revoked, which would materially harm our business, prospects, operating results and financial condition.

Moreover, if we elect or are required to modify, delay, suspend or terminate any clinical trial for our product candidates, the commercial prospects of our product candidates may be harmed and our ability to generate revenue through their sale may be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly.

We face substantial competition, and our operating results will suffer if we fail to compete effectively.

The commercialization of new drugs is competitive, and we may face worldwide competition from major pharmaceutical companies, specialty pharmaceutical companies, biotechnology companies and ultimately generic companies. Our competitors may develop or market therapies that are more effective, safer or less costly than any that we are commercializing, or may obtain regulatory or reimbursement approval for their therapies more rapidly than we may obtain approval for ours.

We are aware of a number of companies that are working to develop drugs that would compete, directly or indirectly, against livoletide for the treatment of hyperphagia in patients with PWS, nevanimibe for the treatment of CAH, and MLE-301 for the treatment of vasomotor symptoms ("VMS").

We are aware of three companies conducting clinical trials seeking to address hyperphagia in patients with PWS. Soleno Therapeutics, Inc. is currently developing diazoxide choline controlled release, an ATP-sensitive potassium channel agonist, and Levo Therapeutics, Inc. is pursuing development of carbetocin, a long-acting analogue of oxytocin. Saniona AB has also announced results of a Phase 2a study in adolescents and adults in PWS for the treatment of hyperphagia. There are also a number of compounds in preclinical development.

We are aware of three other companies developing treatments for patients with CAH: Diurnal Group PLC is developing an exogenous cortisol treatment with a modified release intended to more closely match the physiological release profile of cortisol but recently announced a failed Phase 3 study and placed their United States development activities on hold. Diurnal Group PLC submitted a Market Authorization Application to the EMA in December of 2019. Both Spruce Biosciences, Inc and Neurocrine Biosciences, Inc. are developing CRF1 antagonists and have completed Phase 2 studies in adults with CAH. Neurocrine Biosciences, Inc. has announced the initiation of a Phase 2 study in a pediatric CAH population and announced their intention to start an adult Phase 3 CAH study in mid-2020. Spruce Biosciences has announced intentions to conduct two Phase 2b studies in adults with CAH as well as initiate a pediatric Phase 2 study. BridgeBio Pharma, Inc. is evaluating a gene therapy program (BBP-631) to treat CAH and has announced plans to file an IND in 2020.

We are aware of four competing NK3R antagonists currently in clinical development for VMS. Astellas is developing fezolinetant and has announced the initiation of their Phase 3 VMS program. KaNDy Therapeutics has recently announced preliminary positive topline data for NT-814, a dual NK1/3 receptor antagonist, with full trial results yet to be disclosed. Sojournix is currently studying SJX-653 in a Phase 2 trial. Additionally, Acer Therapeutics has announced their intentions to develop osanetant, an NK3R antagonist, for induced vasomotor symptoms stemming from hormonal therapies used to treat breast and prostate cancer.

Many of our existing or potential competitors may have substantially greater financial, technical and human resources than we do, and significantly greater experience in the discovery and development of product candidates, including in the recruitment of patients for clinical trials, as well as in obtaining regulatory approvals of those product candidates in the United States and in foreign countries. Our current and potential future competitors may also have significantly more experience commercializing drugs that have been approved for marketing. If we are not able to compete effectively against existing and potential competitors, our business and financial condition may be harmed.

Mergers and acquisitions in the pharmaceutical and biotechnology industries could result in even more resources being concentrated among a small number of our competitors. Competition may reduce the number and types of patients available to us to participate in clinical trials, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors.

Competition may further increase as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, drugs that are more effective or less costly than any product candidate that we may develop.

Any inability to successfully complete clinical development of a product candidate could result in additional costs or impair or eliminate our ability to generate revenue from future sales of such product candidate, if approved, or from any regulatory and commercialization milestone with respect to such product candidate. In addition, if we make manufacturing or formulation changes to livoletide or nevanimibe, we may need to conduct additional testing to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize livoletide or nevanimibe, or allow our competitors to bring comparable drugs to market before we do, which could impair our ability to successfully commercialize livoletide or nevanimibe, and may harm our business, financial condition and results of operations.

Established pharmaceutical and biotechnology companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make livoletide, nevanimibe or MLE-301 less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, discovering, developing and receiving FDA or other regulatory authority approval, or commercializing drugs before we do, which would have an adverse impact on our business and results of operations.

The availability of our competitors' products could limit the demand and the price we are able to charge for any product candidate we develop. The inability to compete with existing or subsequently introduced drugs would harm our business, prospects, financial condition and results of operations.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and even if we obtain approval for a product candidate in one country or jurisdiction, we may never obtain approval for, or commercialize, that product candidate in any other jurisdiction, which would limit our ability to realize our full market potential.

Prior to obtaining approval to commercialize a product candidate in any jurisdiction, we or our collaborators must demonstrate with substantial evidence from well controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if our product candidates meet their safety and efficacy endpoints in clinical trials, the FDA or foreign regulatory agencies may believe the clinical trials do not show the appropriate balance of safety and efficacy in the indication being sought or may interpret the data differently than we do, and deem the results insufficient to demonstrate the appropriate balance of safety and efficacy at the level required for product approval. Further, the regulatory authorities may not complete their review processes in a timely manner, or we may otherwise not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

Further, in order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy. Approval by the FDA in the United States does not ensure approval by regulatory authorities in any other country or jurisdiction. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional preclinical studies or clinical trials, which could be costly and time consuming. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

The FDA or any foreign regulatory bodies can delay, limit or deny approval of our product candidates or require us to conduct additional preclinical or clinical testing or abandon a program for many reasons, including:

- the FDA or the applicable foreign regulatory agency's disagreement with the design or implementation of our clinical trials;
- negative or ambiguous results from our clinical trials or results that may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;

- serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that our product candidates are safe and effective for the proposed indication;
- the FDA's or the applicable foreign regulatory agency's disagreement with the interpretation of data from preclinical studies or clinical trials;
- our inability to demonstrate the clinical and other benefits of our product candidates outweigh any safety or other perceived risks;
- the FDA's or the applicable foreign regulatory agency's requirement for additional preclinical studies or clinical trials;
- the FDA's or the applicable foreign regulatory agency's disagreement regarding the formulation, labeling or the specifications of our product candidates;
- the FDA's or the applicable foreign regulatory agency's failure to approve the manufacturing processes or facilities of third-party manufacturers with which we contract, including failure of such manufacturers to pass the required pre-approval inspections; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Even if we eventually complete clinical testing and receive approval of an NDA or foreign marketing application for our product candidates, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials, or the implementation of a Risk Evaluation and Mitigation Strategy, or REMS, which may be required to ensure safe use of the drug after approval. The FDA or the applicable foreign regulatory agency also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and would negatively impact our business and results of operations.

If we are not able to obtain orphan drug designations or exclusivity for any of our current or future product candidates for which we seek such designation, the potential profitability of any such product candidates could be limited.

Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product as an orphan drug if the treatment is 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. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for a disease for which it receives the designation, then the product is entitled to a period of marketing exclusivity that precludes the applicable regulatory authority from approving another marketing application for the same product for the same disease for the exclusivity period except in limited situations. For purposes of small molecule drugs, the FDA defines "same drug" as a drug that contains the same active moiety and is intended for the same use as the drug in question.

We have received orphan drug designation for livoletide from the FDA and EMA for the treatment of hyperphagia in patients with PWS. Nevanimibe has received orphan drug designation from the FDA and the EMA for the treatment of CAH. We may also seek orphan drug designation, where applicable, for our current product candidates in additional indications or for our future product candidates. However, obtaining an orphan drug designation can be difficult and we may not be successful in doing so for any of our current or future product candidates, in any applicable indication. Even if we were to obtain orphan drug designation for a product candidate, we may not obtain orphan exclusivity and that exclusivity may not effectively protect the product candidate from the competition of different products or drugs for the same condition, which could be approved during the exclusivity period. Additionally, after an orphan drug is approved, the FDA could subsequently approve another application for the same product for the same disease if the FDA concludes that the later product is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusive marketing rights in the United States also may be lost if the FDA later determines that the request for designation was materially defective, the prevalence of the orphan disease is found to increase such that the qualifying criterion is no longer met or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. The failure to obtain an orphan drug designation for any

product candidates we may develop and seek it for, the inability to maintain that designation for the duration of the applicable period, or the inability to obtain or maintain orphan drug exclusivity could reduce our ability to make sufficient sales of the applicable product candidates to balance our expenses incurred to develop it, which would have a negative impact on our operational results and financial condition.

If we are not able to obtain required regulatory approvals, we will not be able to commercialize livoletide or nevanimibe, and our ability to generate revenue will be harmed.

Livoletide and nevanimibe and the activities associated with their development and commercialization, including their design, research, testing, manufacture, safety, efficacy, recordkeeping, labeling, packaging, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by similar regulatory authorities outside the United States. Failure to obtain marketing approval for livoletide and nevanimibe or failure to meet post-marketing requirements will prevent us from commercializing them.

We have not yet received approval from regulatory authorities to market any product candidate in any jurisdiction, and it is possible that none of livoletide, nevanimibe or any future product candidates will ever obtain the appropriate regulatory approvals necessary for us to commence product sales. Neither we nor any future collaborator is permitted to market any of our product candidates in the United States until we receive regulatory approval of an NDA from the FDA.

The time required to obtain approval of an NDA by the FDA is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. Prior to submitting an NDA to the FDA or an equivalent application to other foreign regulatory authorities for approval of livoletide for the treatment of hyperphagia in patients with PWS or for approval of nevanimibe for the treatment of CAH, we will need to complete its currently planned registration clinical trials for each, and additional trials that the FDA may require us to complete.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with livoletide or nevanimibe, we may:

- be delayed in obtaining marketing approval for livoletide or nevanimibe, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Furthermore, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions.

We may rely on third-party CROs and consultants to assist us in filing and supporting the applications necessary to gain marketing approvals. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each disease to establish the safety and efficacy of livoletide, nevanimibe and any future product candidate for that disease. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities.

Even if we obtain regulatory approval for livoletide, nevanimibe or future product candidates, we will remain subject to ongoing regulatory oversight.

Even if we obtain any regulatory approval for livoletide, nevanimibe or future product candidates, the approved product will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information. For example, we must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising and the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling. In addition, any regulatory approvals that we receive for livoletide, nevanimibe or future product candidates may also be subject to REMS limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the quality, safety and efficacy of the drug.

In addition, drug manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the NDA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requiring recall or withdrawal of the drug from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of livoletide, nevanimibe or future product candidates, a regulatory authority may, among other things:

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the drug;
- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize livoletide and nevanimibe, and harm our business, financial condition and results of operations.

In addition, the FDA's policies, and those of equivalent foreign regulatory agencies, may change and additional government regulations may be enacted that could suspend or restrict regulatory approval of livoletide and nevanimibe. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would harm our business, financial condition and results of operations.

Even if one of our product candidates receives marketing approval, it may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success.

Even if one of our product candidates receives marketing approval, it may fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If any such product candidate does not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of

market acceptance of a product candidate, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the efficacy and potential advantages compared to alternative treatments;
- the success of our efforts to educate physicians, patients, third-party payors and others in the medical community on the benefits of our products;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- our ability to offer our drugs, once approved, for sale at competitive prices;
- the 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;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement, and patients' willingness to pay out-of-pocket in the absence third-party coverage or adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our drugs, once approved, together with other medications

If the market opportunities for our product candidates are smaller than we believe they are, our product revenues may be adversely affected and our business may suffer.

Our efforts to educate physicians, patients, third-party payors and others in the medical community on the benefits of our products, if and when approved, may require significant resources and may never be successful. Further, patient populations suffering from PWS and CAH, and other indications we may target in the future, are small and have not been established with precision. If the actual number of patients is smaller than we estimate for any disease that we are targeting, or if we cannot raise awareness of these diseases and diagnosis is not improved, our revenue and ability to achieve profitability may be adversely affected. For example, since the patient populations for PWS and CAH are small, the per-patient drug pricing must be high in order to recover our development and manufacturing costs, fund adequate patient support programs and achieve profitability. For PWS and CAH, then, we may not maintain or obtain sufficient sales volume at a price high enough to justify our product development efforts and our sales and marketing and manufacturing expenses. Because we expect sales of livoletide and nevanimibe, if approved, to generate substantially all of our product revenue for the foreseeable future, the failure of either of these product candidates to find market acceptance would harm our business.

If we are unable to establish sales, marketing and distribution capabilities, either on our own or in collaboration with third-parties, we may not be successful in commercializing our product candidates, if approved.

We do not have any infrastructure for the sales, marketing or distribution of our products, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any product that may be approved, we must build our sales, distribution, marketing, managerial and other non-technical capabilities, or make arrangements with third-parties to perform these services. There can be no assurance we will be able to do so in a cost-effective manner, on terms favorable to us, or at all.

While we may seek the aid of global or regional collaborators to provide additional resources for larger indications or to co-commercialize our product candidates in the European Union and certain other territories, we expect to build a focused sales, distribution and marketing infrastructure to market our product candidates in the United States itself, if approved. There are significant expenses and risks involved with establishing our own sales, marketing and distribution capabilities, including our ability to hire, retain and appropriately incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities could delay any product launch, which would adversely impact its commercialization.

Factors that may inhibit our future efforts to commercialize our products on our own include:

- our inability to raise additional capital through equity or debt financings or through lending and licensing arrangements;
- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to educate adequate numbers of physicians as to the benefits or our drug products;
- the inability of reimbursement professionals to negotiate arrangements, for formulary access, reimbursement, and other acceptance by payors;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Further, we do not anticipate having the resources in the foreseeable future to allocate to the sales and marketing of our product candidates in certain markets overseas. Therefore, our future success will depend, in part, on our ability to enter into and maintain collaborative relationships for such capabilities, the collaborator's strategic interest in a product and such collaborator's ability to successfully market and sell the product. We intend to pursue collaborative arrangements regarding the sale and marketing of our product candidates, if approved, for certain markets overseas; however, we cannot assure you that we will be able to establish or maintain such collaborative arrangements, or if able to do so, that we will have effective sales forces. To the extent that we depend on third-parties for marketing and distribution, any revenue we receive will depend upon the efforts of such third-parties, and there can be no assurance that such efforts will be successful.

If we are unable to build our own sales force or negotiate a collaborative relationship for the commercialization of our product candidates, we may be forced to delay our potential commercialization or reduce the scope of our sales or marketing activities for them. If we elect to increase our expenditures to fund commercialization activities itself, we will 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 or generate product revenue. We could enter into arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be ideal and we may be required to relinquish rights to our product candidates or otherwise agree to terms unfavorable to us, any of which may have an adverse effect on our business and results of operations.

If we are unable to establish adequate sales, marketing and distribution capabilities, either on our own or in collaboration with third-parties, we will not be successful in commercializing our product candidates and may not become profitable. We will be competing with many companies that currently have extensive and well-funded sales and marketing operations. Without an internal team or the support of a third-party to perform sales and marketing functions, we may be unable to compete successfully against these more established companies.

Even if we obtain and maintain approval for our current and future product candidates from the FDA, we may nevertheless be unable to obtain approval for our product candidates outside of the United States, which would limit our market opportunities and could harm our business.

Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. If approved, sales of livoletide, nevanimibe and any future product candidate outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries also must approve the manufacturing and marketing of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for any product candidates, if approved, is also subject to approval. Obtaining approval for livoletide, nevanimibe or any future product candidate in the European Union from the European Commission following the opinion of the EMA, if we choose to submit a marketing authorization application there, would be a lengthy and

expensive process. Even if a product candidate is approved, the FDA or the European Commission, as the case may be, may limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of livoletide, nevanimibe or any future product candidate in certain countries.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for livoletide, nevanimibe or any future product candidate may be withdrawn. If we fail to comply with the regulatory requirements, our target market will be reduced and our ability to realize the full market potential of livoletide, nevanimibe or any future product candidate will be negatively impacted, and our business, prospects, financial condition and results of operations could be harmed.

We are exposed to a variety of risks associated with our international operations.

Since the closing date of the Merger, we have been engaged in the process of winding up various subsidiaries of OvaScience, some or all of which are in foreign jurisdictions. We expect to incur additional costs to complete this process. Moreover, even if we successfully wind up these entities, we may be exposed to liability in these foreign jurisdictions as a result of their historical operations.

In addition, in December 2017, we acquired Alizé Pharma SAS ("Alizé"), a biopharmaceutical company based in Lyon, France. As of March 1, 2020, we had 35 employees located in the United States and 3 employees located in France. Our global operations expose us to numerous and sometimes conflicting legal, tax and regulatory requirements, and violations or unfavorable interpretation by the respective authorities of these regulations could harm our business. Risks associated with international operations include the following, and these risks may be more pronounced if we seek to commercialize livoletide, nevanimibe or any future product candidates outside of the United States:

- different regulatory requirements for approval of therapies in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- foreign reimbursement, pricing and insurance regimes;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- changes in diplomatic and trade relationships;
- anti-corruption laws, including the FCPA, and its equivalent in foreign jurisdictions, such as the UK Bribery Act;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires.

In addition, there are complex regulatory, tax, labor, and other legal requirements imposed by both the European Union and many of the individual countries in and outside of Europe, with which we may need to comply. Many biopharmaceutical companies have found the process of marketing their own products in foreign countries to be very challenging.

Furthermore, in some countries, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution or arbitrage between low-priced and high-priced

countries, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies, which is time-consuming and costly. If coverage and reimbursement of our product candidates are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

Legal, political and economic uncertainty surrounding the planned exit of the U.K., from the European Union, or EU, may be a source of instability in international markets, create significant currency fluctuations, adversely affect our operations in the U.K. and pose additional risks to our business, revenue, financial condition, and results of operations.

On June 23, 2016, the U.K. held a referendum in which a majority of the eligible members of the electorate voted for the U.K. to leave the EU. The U.K.'s withdrawal from the EU is commonly referred to as Brexit. The U.K. formally left the EU on January 31, 2020, and is now in a transition period through December 31, 2020. The lack of clarity over which EU laws and regulations will continue to be implemented in the U.K. after Brexit (including financial laws and regulations, tax and free trade agreements, intellectual property rights, data protection laws, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws) may negatively impact foreign direct investment in the U.K., increase costs, depress economic activity and restrict access to capital. The uncertainty concerning the U.K.'s legal, political and economic relationship with the EU after Brexit may be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise) beyond the date of Brexit.

These developments, or the perception that any of them could occur, have had, and may continue to have, a significant adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and limit the ability of key market participants to operate in certain financial markets. In particular, it could also lead to a period of considerable uncertainty in relation to the U.K. financial and banking markets, as well as on the regulatory process in Europe. Asset valuations, currency exchange rates and credit ratings may also be subject to increased market volatility. The long-term effects of Brexit will depend on any agreements (or lack thereof) between the U.K. and the EU and, in particular, any arrangements for the U.K. to retain access to EU markets either during a transitional period or more permanently.

Such a withdrawal from the EU is unprecedented, and it is unclear how the U.K.'s access to the European single market for goods, capital, services and labor within the EU, or single market, and the wider commercial, legal and regulatory environment, will impact us. We may also face new regulatory costs and challenges that could have an adverse effect on our operations. Depending on the terms of the U.K.'s withdrawal from the EU, the U.K. could lose the benefits of global trade agreements negotiated by the EU on behalf of its members, which may result in increased trade barriers that could make our doing business in the U.K. more difficult. Furthermore, there are likely to be changes to the way in which marketing approvals are granted in the U.K., which could add time and expense to the process by which our product candidates receive and maintain regulatory approval in the U.K. and across the European Economic Area in future.

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

We face an inherent risk of product liability exposure related to the testing of our current and future product candidates, and may face an even greater risk if we commercialize any product candidate that it may develop. If we cannot successfully defend ourselves against claims that any such product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidate that we may develop;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend the related litigation;
- withdrawal of clinical trial participants;
- the inability to commercialize any product candidate that it may develop;
- injury to our reputation and significant negative media attention; and
- increased marketing costs to attempt to overcome any injury to our reputation or negative media attention.

In addition, we face an inherent risk of product liability exposure related to OvaScience's prior use of fertility treatments in humans. Product liability claims involving OvaScience's activities may be brought for significant amounts because OvaScience's potential fertility treatments involved mothers and children. For example, it is possible that we will be subject to product liability claims that assert that OvaScience's potential fertility treatments have caused birth defects in children or that such defects are inheritable. These claims could be made many years into the future based on effects that were not observed or observable at the time of birth. If we cannot successfully defend against claims that OvaScience's potential fertility treatments caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in, among other things, significant costs to defend the related litigation; substantial monetary awards or payments to trial participants or patients; loss of revenue; and the diversion of management's resources.

Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. 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 liability that may arise.

If OvaScience failed 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.

OvaScience is 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. OvaScience's prior operations involved the use of hazardous and flammable materials, including chemicals and biological materials. OvaScience's prior operations also produced hazardous waste products. OvaScience generally contracted with third-parties for the disposal of these materials and wastes. In the event of contamination or injury resulting from OvaScience's 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.

We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with OvaScience's storage or disposal of biological, hazardous or radioactive materials.

Risks Related to Regulatory Compliance

Our current and future relationships with investigators, health care professionals, consultants, third-party payors and customers may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Our operations may be directly, or indirectly through our prescribers, customers and purchasers, subject to various federal and state fraud and abuse laws and regulations, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and Physician Payments Sunshine Act and regulations. These laws may constrain our current and future business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to patient privacy laws by both the federal government and the states and other countries in which we conduct our business. The laws that will affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, in return for the purchase, recommendation, leasing or furnishing of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand, and prescribers, purchasers, formulary managers, and others on the other hand. In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively PPACA, amended the intent requirement of the federal Anti-Kickback Statute, establishing that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;
- federal civil and criminal false claims laws, including the federal civil False Claims Act, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid or other government payors that are false or fraudulent. PPACA provides, and recent government cases against pharmaceutical and medical device

manufacturers support the view, that federal Anti-Kickback Statute violations and certain marketing practices, including off-label promotion, may implicate the federal civil False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal civil and criminal statutes that prohibit a person from knowingly and willfully executing a scheme or from making false or fraudulent statements to defraud any healthcare benefit program, regardless of the payor (e.g., public or private);
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, health care clearinghouses and certain health care providers, known as covered entities, and their business associates who create, use or disclose individually identifiable health information on their behalf;
- federal transparency laws, including the federal Physician Payments Sunshine Act, that require certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to CMS information related to: (i) payments or other "transfers of value" made to physicians, as defined by such law, and teaching hospitals and (ii) ownership and investment interests held by physicians and their immediate family members;
- state and foreign law equivalents of each of the above federal laws, such as state anti-kickback, self-referral, and false claims laws which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical manufacturers to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts payments that may be made to healthcare providers; state laws that require pharmaceutical manufacturers to file reports with states regarding marketing information, such as the tracking and reporting of gifts, compensation and other remuneration and items of value provided to healthcare professionals and entities; state laws that require the reporting of information related to drug pricing; and state and local laws requiring the registration of pharmaceutical sales representatives; and
- state and foreign laws that govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third-parties will comply with applicable healthcare laws and regulations will involve substantial costs. However, because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the laws described above or any other government regulations that apply to us, we may be subject to penalties, including significant administrative, civil and criminal penalties, damages, fines, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, exclusion from participation in government health care programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm and the curtailment or restructuring of our operations, any of which could harm our ability to operate our business and our results of operations. Similar sanctions and penalties, as well as imprisonment, also can be imposed upon executive officers and employees, including criminal sanctions against executive officers under the so-called "responsible corporate officer" doctrine, even in situations where the executive officer did not intend to violate the law and was unaware of any wrongdoing.

The risk of us being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and its provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain a robust and expandable system to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company such as we may run afoul of one or more of the requirements.

Coverage and adequate reimbursement may not be available for our current or future product candidates, which could make it difficult for us to sell them profitably, if approved.

Market acceptance and sales of any product candidates that we commercialize, if approved, will depend in part on the extent to which coverage and reimbursement for these drugs and related treatments will be available from third-party payors, including government health administration authorities and private health insurers. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a plan-by-plan basis. As a result, the coverage determination process is often a time-consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained. One payor's determination to provide coverage for a drug does not assure that other payors will also provide coverage, and adequate reimbursement, for the drug. Additionally, a third-party payor's decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Each plan determines whether it will provide coverage for a therapy, what amount it will pay the manufacturer for the therapy, and on what tier of its formulary it will be placed. The position on a formulary generally determines the co-payment that a patient will need to make to obtain the therapy and can strongly influence the adoption of such therapy by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our drugs unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our drugs.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand for, or the price of, any drug for which we obtain marketing approval. If coverage and reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize livoletide, nevanimibe and any future product candidates that we develop.

Additionally, there have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell any future product candidates profitably. These legislative and regulatory changes may negatively impact the coverage and available reimbursement for livoletide, nevanimibe and any future product candidates we may commercialize, following approval, if obtained.

Healthcare legislative reform measures may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In March 2010, PPACA was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. PPACA, among other things: (i) addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; (ii) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations; (iii) established annual fees and taxes on manufacturers of certain branded prescription drugs; (iv) expanded the availability of lower pricing under the 340B drug pricing program by adding new entities to the program; and (v) established a new Medicare Part D coverage gap discount program, in which manufacturers must, as of January 1, 2019, agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

There remain judicial and Congressional challenges to certain aspects of PPACA, as well as efforts by the Trump administration to repeal or replace certain aspects of PPACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of PPACA or otherwise circumvent some of the requirements for health insurance mandated by PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of PPACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under PPACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or Tax Act, included a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, the 2020 federal spending package permanently eliminated,

effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the PPACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". In December 2018 CMS published a new final rule permitting further collections and payments to and from certain PPACA qualified health plans and health insurance issuers under the PPACA risk adjustment program. On December 14, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the PPACA will impact the PPACA. We continue to evaluate the potential impact of PPACA and its possible repeal or replacement on our business.

We expect that PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we are able to charge for any approved drug in the United States. For example, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Further, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning on January 1, 2020. The final rule codified a CMS policy change that was effective January 1, 2019. 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, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, such measures are designed to encourage importation from other countries and bulk purchasing. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In addition, other legislative changes have been adopted since PPACA was enacted. These changes include aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, following passage of the Bipartisan Budget Act of 2018, among other legislative amendments, will remain in effect through 2029 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and, accordingly, our financial operations.

Additional changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under the health insurance exchanges and fraud and abuse and enforcement. Continued implementation of PPACA and the passage of additional laws and regulations may result in the expansion of new programs such as Medicare payment for performance initiatives, and may impact existing government healthcare programs, such as by improving the physician quality reporting system and feedback program. For each state that does not choose to expand its Medicaid program, there likely will be fewer insured patients overall, which could impact the sales, business and financial condition of manufacturers of branded prescription drugs. Where patients receive insurance coverage under any of the new options made available through PPACA, the possibility exists that manufacturers may be required to pay Medicaid rebates on their resulting drug utilization, a decision that could impact manufacturer revenues.

Regulatory, legislative or self-regulatory/standard developments regarding privacy and data security matters could adversely affect our ability to conduct our business.

We are subject to and affected by laws, rules, regulations and industry standards related to data privacy and security, and restrictions or technological requirements regarding the collection, use, storage, security, retention or transfer of data. In the United States, the rules and regulations to which we may be subject include federal laws and regulations enforced by the Federal Trade Commission, the Department of Health & Human Services, and state privacy, data security, and breach notification laws, as well as regulator enforcement positions and expectations. Internationally, governments and agencies have adopted and could in the future adopt, modify, apply or enforce additional laws, policies, regulations, and standards covering privacy and data security that may apply to our business. New regulation or legislative actions regarding data privacy and security (together with applicable industry standards) may increase our costs of doing business. In addition to privacy and data security regulations currently in force in the jurisdictions where we operate, the European Union General Data Protection Regulation, or GDPR, went into effect in May 2018. The GDPR contains numerous requirements and changes from existing European Union, or EU, law, including more robust obligations on data processors and data controllers and heavier documentation requirements for data protection compliance programs. Specifically, the GDPR will introduce numerous privacy-related changes for companies operating in the EU, including greater control over personal data-by-data subjects (e.g., the "right to be forgotten"), increased data portability for EU consumers, data breach notification requirements, and increased fines. In particular, under the GDPR, fines of up to €20 million or up to 4% of the annual global revenue of the noncompliant company, whichever is greater, could be imposed for violations of certain of the GDPR's requirements. The GDPR requirements apply not only to third-party transactions, but also to transfers of information between us and our subsidiaries, including employee information. However, despite our ongoing efforts to bring our practices into compliance before the effective date of the GDPR, we may not be successful either due to various factors within our control, such as limited financial or human resources, or other factors outside our control. It is also possible that local data protection authorities may have different interpretations of the GDPR, leading to potential inconsistencies amongst various EU member states. Any failure or alleged failure (including as a result of deficiencies in our policies, procedures, or measures relating to privacy, data security, marketing, or communications) by us to comply with laws, regulations, policies, legal or contractual obligations, industry standards, or regulatory guidance relating to privacy or data security, may result in governmental investigations and enforcement actions, litigation, fines and penalties, additional regulatory oversight and reporting obligations or adverse publicity. We expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the United States, the European Union, and in other jurisdictions, and we cannot determine the impact such future laws, regulations and standards may have on our business.

Future laws, regulations, standards and other obligations or any changed interpretation of existing laws or regulations could impair our ability to operate our business and negatively impact our results of operations.

Risks Related to Our Intellectual Property

We rely on the availability of licenses for intellectual property from third-parties and these licenses may not be available to us on commercially reasonable terms, or at all.

We rely upon the UM License Agreement to certain patent rights and proprietary technology from the University of Michigan that are important or necessary to the development of nevanimibe. We rely upon the Roche License Agreement to certain patent rights and proprietary technology from Roche that are important or necessary to the development of MLE-301. As of December 31, 2019, with respect to nevanimibe patent rights, we owned two issued U.S. patents, two pending U.S. patent applications, and a number of patent applications in other jurisdictions, and we jointly owned, with the University of Michigan, three issued U.S. patents, one pending U.S. patent application, and a number of patent applications in other jurisdictions. In addition, as of December 31, 2019, with respect to livoletide patent rights, we owned four issued U.S. patents, one pending U.S. patent application, and a number of patents and pending patent applications in other jurisdictions. Finally, as of December 31, 2019, with respect to MLE-301 patent rights, we owned one pending U.S. patent application, and we exclusively licensed from Roche one issued U.S. patent and a number of patents and pending patent applications in other jurisdictions. There is no guarantee that any of the foregoing patent applications will result in issued patents, or that any current patents or patent applications, if issued, will include claims that are sufficiently broad to cover our product candidates or future products, or to provide meaningful protection from our competitors in all territories in which we may wish to develop or commercialize our products in the future. We will be able to protect our proprietary rights from unauthorized use by third-parties only to the extent they are covered by valid and enforceable patents or are effectively maintained as trade secrets within our organization. If third-parties disclose or misappropriate our proprietary rights, it may have a material adverse effect on our business.

The licenses granted under the UM License Agreement and Roche License Agreement, respectively, are revocable under certain circumstances including if we cease to do business, fail to make the payments due thereunder, commit a material breach

of the agreement that is not cured within a certain time period after receiving written notice or fail to meet certain specified development and commercial timelines. In such an event, our ability to compete in the market for a particular drug indication may be diminished. Termination of the UM License Agreement or Roche License Agreement may result in us having to negotiate a new or reinstated agreement, which may not be available to us on equally favorable terms, or at all, which may mean we are unable to develop or commercialize nevanimibe or MLE-301, as applicable. Additionally, the UM License Agreement, Roche License Agreement and other licenses we may enter into in the future may not provide exclusive rights to use such intellectual property and technology at all, in all relevant fields of use and/or in all territories in which we may wish to develop or commercialize our product candidates in the future. As a result, we may not be able to prevent competitors from developing and commercializing competitive products, including in territories included in the UM License Agreement and Roche License Agreement.

Licenses to additional third-party patents and materials that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could harm our business and financial condition.

Our intellectual property licenses and agreements with third-parties may be subject to disagreements over contract interpretation, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

We currently depend, and will continue to depend, on the UM License Agreement. In addition, pursuant to an assignment agreement for certain patents and patent applications relating to livoletide, we are also required to pay royalties on commercial sales and licensing of livoletide to the assignors. Further, the assignors under this assignment agreement have a right to repurchase the assigned intellectual property at a certain price in the event we do not, upon receiving notice, use reasonable efforts to develop, introduce for sale and promote products derived from the assigned intellectual property. Such reasonable efforts involve spending an annual amount of at least CDN$100,000 in research and development related to livoletide, actively pursuing the registration, licenses and permits necessary to market livoletide and actual commercialization of livoletide, if approved. We currently depend, and will continue to depend, on the Roche License Agreement. If Roche terminates the Roche License Agreement due to a breach of any of our material obligations under the Roche License Agreement or due to our insolvency, or if we terminate the Roche License Agreement without cause, the rights and licenses granted by Roche to us under the Roche License Agreement will terminate on the effective date of the termination. In such event, if Roche provides us with timely notice, and to the extent reasonably requested by Roche, we must transfer to Roche all regulatory filings and approvals, all final preclinical, non-clinical and clinical study reports and clinical study protocols, trademarks, and all data, including clinical data, materials and information, in our possession and control related to MLE-301 necessary or reasonably useful for Roche to continue to develop and commercialize MLE-301. Further, if the effective date of such a termination is after the first commercial sale of the first MLE-301 product, Roche shall have a worldwide, non-exclusive, sublicensable, transferable license to research, develop, manufacture, and sell MLE-301 compounds and products. In such event, Roche would pay to us royalty fees with respect to the sale of those compounds and products. Further development and commercialization of livoletide, nevanimibe and MLE-301 may, and development of any future product candidates may, require us to enter into additional license, assignment or collaboration agreements. The agreements under which we currently hold or license intellectual property or technology from third-parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

If any of our current or future licenses or agreements or material relationships or any in-licenses upon which our current or future licenses and intellectual property are based are terminated or breached, we may:

- lose our rights to develop and market our current and any future product candidates;
- lose our rights to patent protection for our current or any future product candidates;
- experience significant delays in the development or commercialization of our current or any future product candidates;
- not be able to obtain any other licenses on acceptable terms, if at all; or
- incur liability for damages.

These risks apply to any agreements that we may enter into in the future for livoletide, nevanimibe, MLE-301 or for any future product candidates. If we experience any of the foregoing, it would have a material adverse effect on our business, financial condition and results of operations.

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

Further, we cannot provide any assurances that third-party patents or other intellectual property rights do not exist, which might be enforced against our current product candidates, resulting in either an injunction prohibiting our manufacture or sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third-parties. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, prospects, financial condition and results of operations.

If we are unable to obtain and maintain patent protection for our technology and products, or if the scope of the patent protection obtained is not sufficiently broad, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates. Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our current and future product candidates in the United States and other countries in which we plan to develop and commercialize such product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our development programs and product candidates. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

Pursuant to the UM License Agreement, we obtained an exclusive, worldwide license to develop, manufacture and commercialize nevanimibe. However, the UM License Agreement permits the University of Michigan, and other non-profit research institutions which are granted such rights from the University of Michigan, to manufacture and research nevanimibe for internal research, public service and internal educational purposes, all of which could result in new patentable inventions concerning the manufacture or use of nevanimibe. In addition, pursuant to an assignment agreement for certain livoletide patents and patent applications, certain individuals at the Erasmus University Medical Center and the University of Turin were granted non-exclusive rights to use the assigned intellectual property for non-commercial research with our prior written consent, all of which could result in new patentable inventions concerning the manufacture or use of livoletide. Pursuant to the Roche License Agreement, we obtained an exclusive, worldwide license to develop, manufacture and commercialize MLE-301. However, the Roche License Agreement permits Roche to use MLE-301 for internal research purposes, which could result in new patentable inventions concerning the manufacture or use of MLE-301.

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 applications that we own or in-license may fail to result in issued patents with claims that cover our current and future product candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our current and future product candidates, third-parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated or held unenforceable. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate and companion diagnostic under patent protection could be reduced.

If the patent applications we hold or have in-licensed with respect to our development programs and product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our current and future product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize future drugs. Any such outcome could have a material adverse effect on our business.

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. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Further, we may not be aware of

all third-party intellectual property rights potentially relating to our product candidates. Publications of discoveries in scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically published 18 months after filing, or in some cases, not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and drugs. 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.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The United States Patent and Trademark Office, or USPTO, recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. Any further 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 and patent applications or narrow the scope of our potential patent protection.

Moreover, we may be subject to a third-party pre-issuance submission of prior art to the USPTO or become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third-parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize product candidates without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

The issuance of a patent is not conclusive as to its inventorship, 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 loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and product candidates, or limit the duration of the patent protection of our technology and product candidates. Moreover, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years from the earliest filing date of a non-provisional patent application. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our current or future product candidates, we may be open to competition from generic versions of such drugs. 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, we owned and licensed patent portfolio may not provide it with sufficient rights to exclude others from commercializing drugs similar or identical to that of us.

We jointly own patents and patent applications with third-parties. Our ability to exploit or enforce these patent rights, or to prevent the third-party from granting licenses to others with respect to these patent rights, may be limited in some circumstances.

We jointly own certain patents and patent applications with third-parties. In the absence of an agreement with each co-owner of jointly owned patent rights, we will be subject to default rules pertaining to joint ownership. Some countries require the consent of all joint owners to exploit, license or assign jointly owned patents, and if we are unable to obtain that consent from the joint owners, we may be unable to exploit the invention or to license or assign our rights under these patents and patent applications in those countries. For example, we secured exclusive rights from the University of Michigan for certain patents and patent applications that they jointly own with us related to nevanimibe. Additionally, in the United States, each co-owner may be required to be joined as a party to any claim or action we may wish to bring to enforce these patent rights, which may limit our ability to pursue third-party infringement claims.

We have in-licensed patents and patent applications from third-parties. Our ability to exploit or enforce these patent rights, or to prevent the third-party from granting licenses to others with respect to these patent rights, may be limited in some circumstances.

We have in-licensed certain patents and patent applications from third-parties. In the absence of an agreement with each patent rights owner, we will be subject to default rules pertaining to ownership. Some countries require the consent of all owners to exploit, license or assign owned patents, and if we are unable to obtain that consent from the owners, we may be unable to exploit the invention or to license or assign our rights under these patents and patent applications in those countries. For example, we secured exclusive rights from Roche for certain patents and patent applications that they own related to MLE-301. Additionally, in the United States, each owner may be required to be joined as a party to any claim or action we may wish to bring to enforce these patent rights, which may limit our ability to pursue third-party infringement claims.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the United States in several stages over the lifetime of our owned and licensed patents and/or applications and any patent rights it may own or license in the future. We rely on our outside counsel or our licensing partners to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules.

There are situations, however, in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction.

In such an event, potential competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of new product candidates such as livoletide, nevanimibe and MLE-301, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits extension of the term of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved drug, an FDA-approved method of treatment using the drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. Further, we may not elect to extend the most beneficial patent to us or the claims underlying the patent that we choose to extend could be invalidated. If any of the foregoing occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing its clinical and preclinical data and launch their drug earlier than might otherwise be the case.

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

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business. The following examples are illustrative:

- others may be able to make compounds, or livoletide, nevanimibe or MLE-301 formulations that are similar to our livoletide, nevanimibe or MLE-301 formulations but that are not covered by the claims of the patents that we own or control;

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

We do not have broad composition of matter patent protection with respect to nevanimibe.

We own certain patents and patent applications with claims directed to a form of nevanimibe and to specific methods of using nevanimibe and we expect to have marketing exclusivity from the FDA and EMA for a period of seven and ten years, respectively, because nevanimibe has not been approved in these markets. However, we do not have composition of matter protection in the United States and elsewhere broadly covering nevanimibe. We may be limited in our ability to list our patents in the FDA's Orange Book if the form of the compound used is materially different from what is claimed in our patents, or if the use of its product, consistent with its FDA-approved label, would not fall within the scope of our patent claims. Also, our competitors may be able to offer and sell products so long as these competitors do not infringe any other patents that we (or third-parties) hold, including patents with claims directed to the forms and manufacture of nevanimibe and/or method of use patents. In general, patents covering certain forms of a compound and method of use patents are more difficult to enforce than broad composition of matter patents because, for example, of the risks that the FDA may approve different forms of subject compounds or alternative uses of the subject compounds not covered by the method of use patents, and others may engage in off-label sale or use of the subject compounds. Physicians are permitted to prescribe an approved product for uses that are not described in the product's labeling. Although off-label prescriptions may infringe its method of use patents, the practice is common across medical specialties and such infringement is difficult to prevent or prosecute. FDA approval of uses that are not covered by our patents would limit our ability to generate revenue from the sale of nevanimibe, if approved for commercial sale. Off-label sales would limit our ability to generate revenue from the sale of nevanimibe, if approved for commercial sale.

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

Our commercial success depends, in part, upon our ability, and the ability of our future collaborators, to develop, manufacture, market and sell livoletide, nevanimibe, MLE-301 and any future product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third-parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to livoletide, nevanimibe, MLE-301 and any future product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Third-parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third-parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could have a material adverse effect on our ability to commercialize livoletide, nevanimibe, MLE-301 and any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If we are found to infringe a third-party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third-party to continue developing,

manufacturing and marketing our product candidate 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 and other third-parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidate. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. A finding of infringement could prevent us from manufacturing and commercializing livoletide, nevanimibe, MLE-301 or any future product candidates or force us to cease some or all of our business operations, which would have a material adverse effect on our business. Claims that we have misappropriated the confidential information or trade secrets of third-parties could have a similar material adverse effect on our business. Even if we prevail in such infringement claims, patent litigation can be expensive and time consuming, which would harm our business, financial condition and results of operations.

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

Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of ours patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. The initiation of a claim against a third-party may also cause the third-party to bring counter claims against us such as claims asserting that our patents are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third-parties may also raise similar validity claims before the USPTO in post-grant proceedings such as ex parte reexaminations, inter partes review, or post-grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third-party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could have material adverse effect on our business.

We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees. Even if we prevail in such infringement claims, patent litigation can be expensive and time consuming, which would harm our business, financial condition and results of operations.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common stock.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

The United States has recently enacted and implemented wide-ranging patent reform legislation. The U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, federal courts, USPTO, and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce patents that we have licensed or that we might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions or changes in the governmental bodies that enforce them or changes in

how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we have licensed or that we may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world, which could have a material adverse effect on our business.

Filing, prosecuting and defending patents covering livoletide, nevanimibe, MLE-301 and any future product candidates throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop our own drugs and, further, may export otherwise infringing drugs to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These drugs may compete with our drugs in jurisdictions where we do not have any issued or licensed patents and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Our reliance on third-parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

If we rely on third-parties to manufacture and commercialize livoletide, nevanimibe, MLE-301 or any future product candidates, or if we collaborate with third-parties for the development of livoletide, nevanimibe, MLE-301 or any future product candidates, we must, at times, share trade secrets with them. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third-parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third-parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third-parties, independent development or publication of information by any of third-party collaborators. A competitor's discovery of our trade secrets would harm our business.

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

Certain of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or 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.

In addition, while it is our approach to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third-parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

Risks Related to Our Dependence on Third-Parties

We do not have our own manufacturing capabilities and will rely on third-parties to produce clinical and commercial supplies of livoletide and nevanimibe, and any future product candidate.

We have no experience in drug formulation or manufacturing and do not own or operate, and we do not expect to own or operate, facilities for product manufacturing, storage and distribution, or testing. We will rely on a contract manufacturing organization, or CMO, to produce additional livoletide active pharmaceutical ingredient, or API, for us for clinical use. We also currently rely on CMOs to produce nevanimibe for our clinical trials. Additionally, we rely on CMOs with respect to the manufacture of drug product for our clinical trials, including for filing and packaging. Any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replenish the supply or replace a third-party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates. If we or our manufacturer are unable to purchase these raw materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenue from the sale of our product candidates.

We will need to rely on third-party manufacturers to supply us with sufficient quantities of livoletide and nevanimibe to be used, if approved, for the commercialization of each. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMP requirements for manufacture of drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Further, our reliance on third-party manufacturers entails risks, to which we would not be subject if we manufactured product candidates ourselves, including:

- inability to meet our product specifications and quality requirements consistently;
- delay or inability to procure or expand sufficient manufacturing capacity;
- issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- failure to comply with cGMP and similar foreign standards;
- inability to negotiate manufacturing agreements with third-parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third-parties in a manner or at a time that is costly or damaging to us;
- reliance on a limited number of sources, and in some cases, single sources for product components;
- lack of qualified backup suppliers for those materials that are currently purchased from a sole or single source supplier;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- inability to find replacement manufacturers or suppliers, if necessary, on terms favorable to us, in a timely manner, or at all;
- carrier disruptions or increased costs that are beyond our control; and
- failure to deliver our products under specified storage conditions and in a timely manner.

Any of these events could lead to clinical trial delays, failure to obtain regulatory approval or impact our ability to successfully commercialize our products once approved. Some of these events could be the basis for FDA or other regulatory authority action, including injunction, recall, seizure, or total or partial suspension of production.

We may in the future enter into collaborations with third-parties to develop our product candidates. If these collaborations are not successful, our business could be harmed.

We may enter into collaborations with third-parties in the future. We may in the future determine to collaborate with other pharmaceutical and biotechnology companies for development and potential commercialization of our product candidates. These relationships, or those like them, may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we could face significant competition in seeking appropriate collaborators and the negotiation process is time-consuming and complex. Our ability to reach a definitive collaboration agreement will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of several factors. If we license rights to our product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture.

If any such potential future collaborations do not result in the successful development and commercialization of product candidates, or if one of our future collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, the development of our product candidates could be delayed and we may need additional resources to develop our product candidates. In addition, if one of our future collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, regulatory approval and commercialization apply to the activities of our potential future collaborators.

We may not be successful in finding strategic collaborators for continuing development of livoletide or nevanimibe, or successfully commercializing or competing in the market for certain diseases.

We may seek to develop strategic partnerships for developing and commercializing livoletide or nevanimibe, due to capital costs required to develop the product candidate, manufacturing constraints or anticipated commercialization costs. We may not be successful in our efforts to establish such a strategic partnership or other alternative arrangements for livoletide or nevanimibe because our research and development pipeline may be insufficient or third-parties may not view livoletide or nevanimibe as having the requisite potential to demonstrate safety and efficacy. In addition, we may be restricted under an existing collaboration agreement from entering into a future agreement with a potential collaborator. We cannot be certain that, following a strategic transaction or license, we will achieve an economic benefit that justifies such transaction.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of our product candidates, reduce or delay the development programs, delay potential commercialization, reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop livoletide or nevanimibe, which could harm our business, financial condition and results of operations.

We rely on third-parties to conduct, supervise and monitor our clinical trials, and if those third-parties perform in an unsatisfactory manner, it may harm our business.

We currently do not have the ability to independently conduct preclinical studies and clinical trials that comply with the regulatory requirements known as good laboratory practice, or GLP, or GCP, respectively. We also do not currently have the ability to independently conduct large clinical trials. We intend to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and we expect to have limited influence over their actual performance.

We intend to rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future preclinical studies. We expect to control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our studies or trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs will be required to comply with GLP and GCP, which are regulations and guidelines enforced by the FDA and are also required by the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for any of our product candidates that are in preclinical and clinical development, respectively. The regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and clinical trial sites. Although we rely on CROs to conduct any future GLP-compliant preclinical and preclinical studies and current or planned GCP-compliant clinical trials, we remain responsible for ensuring that each of our GLP preclinical studies and clinical trials is conducted in accordance with our investigational plan and protocol and applicable laws and regulations, and our reliance on the CROs does not relieve us of our regulatory responsibilities. If we or our CROs fail to comply with GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the regulatory approval process.

While we will have agreements governing their activities, our CROs are and will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and preclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our business. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to its clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

If our relationships with these CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can negatively impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business and financial condition. Further, we currently rely on several CROs to conduct our ongoing clinical trials and may engage one of these same CROs to conduct additional clinical trials on our behalf. To the extent that these CROs fail to comply with GLP or their contractual obligations to us for any reason, the negative impact on our business and financial condition could be more profound than if we relied on a greater number of CROs.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

Recent acquisitions and potential future acquisitions could prove difficult to integrate, disrupt our business, dilute stockholder value and strain our resources.

We completed our acquisition of Alizé through which we acquired livoletide, our PWS product candidate, in December 2017. In the future, we may acquire additional companies, technologies or product candidates that we believe could complement or expand our business. Integrating the operations of acquired businesses successfully or otherwise realizing any of the anticipated benefits of acquisitions involves a number of potential challenges. The failure to meet these integration challenges could seriously harm our financial condition and results of operations. Realizing the benefits of acquisitions depends in part on the integration of operations and personnel. These integration activities are complex and time-consuming, and we may encounter unexpected difficulties or incur unexpected costs, including with respect to:

- diversion of management attention from ongoing business concerns to integration matters;
- coordinating clinical and preclinical development plans;
- consolidating and rationalizing information technology and accounting platforms and administrative infrastructures;
- complexities associated with managing the geographic separation of the combined businesses and consolidating multiple physical locations;
- discontinuation of operations of OvaScience and contingent liabilities we assumed in connection with the Merger;

- reconciling different corporate cultures; and
- retaining scientific and other key employees.

Acquired businesses may have liabilities, adverse operating issues or other matters of concern arise following the acquisition that we fail to discover through due diligence prior to the acquisition. Further, our acquisition targets may not have as robust internal controls over financial reporting as would be expected of a public company. Acquisitions may also result in the recording of goodwill and other intangible assets that are subject to potential impairment in the future that could harm our financial results. We may also become subject to new regulations as a result of an acquisition, including if we acquire operations in a country in which we do not already operate. If we fail to properly evaluate acquisitions or unanticipated issues arise following the acquisition, we may incur costs in excess of what we anticipate and may not otherwise achieve the anticipated benefits of any such acquisitions.

We are highly dependent on the services of our key executives and personnel, including Julia C. Owens, Ph.D., our chief executive officer, Christophe Arbet-Engels, our chief medical officer, and Ryan Zeidan, Ph.D., our chief development officer, and if we are not able to retain these members of our management team or recruit and retain additional management, clinical and scientific personnel, our business will be harmed.

We are highly dependent on Drs. Owens, Arbet-Engels, and Zeidan. The employment agreements we have with these officers do not prevent such persons from terminating their employment with us at any time. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

In addition, we are dependent on our continued ability to attract, retain and motivate highly qualified additional management, clinical and scientific personnel. If we are not able to retain our management and to attract, on acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow.

We may not be able to attract or retain qualified personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. Many of the other pharmaceutical companies that we compete against for qualified personnel and consultants have greater financial and other resources, different risk profiles, are located in geographies with a larger biotechnology industry presence and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates and consultants than what we have to offer. If we are unable to continue to attract, retain and motivate high-quality personnel and consultants to accomplish our business objectives, the rate and success at which we can discover and develop product candidates and our business will be limited and we may experience constraints on our development objectives.

Our future performance will also depend, in part, on our ability to successfully integrate newly hired executive officers into our management team and our ability to develop an effective working relationship among senior management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations. Additionally, we do not currently maintain "key person" life insurance on the lives of our executives or any of our employees.

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

As of March 1, 2020, we had 38 employees, 37 of whom were full-time employees and 1 of whom was a part-time employee. As our development and commercialization plans and strategies develop, we expect to need additional managerial, operational, sales, marketing, financial, legal and other resources. Our management may need to divert a disproportionate amount of our attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational inefficiencies, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of our current and future product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and grow revenue could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize our product candidates, develop a scalable infrastructure and compete effectively will depend, in part, on our ability to effectively manage any future growth.

Our employees, independent contractors, principal investigators, consultants, commercial collaborators, service providers and other vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in other jurisdictions, provide accurate information to the FDA and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us and we are not successful in defending itself or asserting our rights, those actions could have a negative impact on our business, financial condition and results of operations, including the imposition of significant fines or other sanctions.

We may be delayed in our receipt of certain tax benefits that Alizé historically received as a French technology company.

As a French technology company, Alizé historically benefited from certain tax advantages, including the French research tax credit (*credit d'impot recherche*), or CIR. The CIR is a French tax credit aimed at stimulating research and development, and can offset French corporate income tax due. Alizé has historically received CIR reimbursements promptly following filing for such reimbursements with applicable French taxing authorities. For the year ended December 31, 2017, claims were made totaling $1.0 million, which we received in the first quarter of 2019. For the year ended December 31, 2018, claims were made totaling $1.3 million, which we received in the third quarter of 2019. We anticipate filing claims totaling $1.3 million for the year ended December 31, 2019. In the future, we may no longer qualify as a French small or medium size enterprise, and, accordingly, we may be subject to a three-year waiting period for reimbursement of CIRs, which could adversely affect the combined business's results of operations and cash flows. In addition, the amount of CIR received is, among other factors, dependent upon incurring qualified research and development expenses related to employee salaries and other personnel costs in France. As a result, if the number of our research and development employees in France decreases, as it did for the year ended December 31, 2019, the amount of CIR we are eligible for would likely decrease.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we are not aware of any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

We may be exposed to significant foreign exchange risk.

We incur portions of our expenses, and may in the future derive revenue, in currencies other than the U.S. dollar, in particular, the euro. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the euro. Therefore, for example, an increase in the value of the euro against the U.S. dollar could be expected to have a negative impact on our operating expenses as euro denominated expenses, if any, would be translated into U.S. dollars at an increased value. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows.

Risks Related to Ownership of Our Common Stock and Our Status as a Public Company

The trading price of the shares of our common stock may be volatile, and purchasers of our common stock could incur substantial losses.

Our stock price may be volatile. The stock market in general and the market for biopharmaceutical 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, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- the commencement, enrollment or results of our clinical trials or changes in the development status of our product candidates;
- any delay in our regulatory filings for any product candidate we may develop, and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- adverse results from, delays in or termination of clinical trials;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- unanticipated serious safety concerns related to the use of our product candidates;
- changes in financial estimates by us or by any securities analysts who might cover our stock;
- conditions or trends in our industry;
- changes in the structure of healthcare payment systems;
- changes in the market valuations of similar companies;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that equity research analysts publish about us and our business. As a newly public company, we have only limited research coverage by equity research analysts. Equity research analysts may elect not to initiate or continue to provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. Even if we continue to have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

Future sales of our common stock in the public market could cause our share price to decline.

Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to the restrictions and limitations described below. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales, particularly sales by our directors, executive officers, and significant stockholders, may have on the prevailing market price of our common stock. As of March 1, 2020, we had 18,266,545 shares of common stock outstanding. All of our outstanding shares of common stock are available for sale in the public market, subject only to the restrictions of Rule 144 under the Securities Act. In addition, the shares of common stock subject to outstanding options under our equity incentive plans and the shares reserved for future issuance under our equity incentive plans will become eligible for sale in the public market in the future, subject to certain legal and contractual limitations. In addition, certain holders of our common stock have the right, subject to various conditions and limitations, to request we include their shares of our common stock in registration statements we may file relating to our securities.

Provisions in our certificate of incorporation and by-laws 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 certificate of incorporation and by-laws 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 common stockholders might otherwise receive a premium price 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, because our board of directors is responsible for appointing the members of our management team, 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. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and for nominations to our board of directors;
- limit who may call stockholder meetings;
- prohibit actions by our stockholders by written consent;
- require that stockholder actions be effected at a duly called stockholders meeting;
- 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 percent of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our certificate of incorporation or by-laws.

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 15 percent or more 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 15 percent or more of our outstanding voting stock, unless the merger or combination is approved in a manner prescribed by the statute.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent our other stockholders from influencing significant corporate decisions.

As of March 1, 2020 our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates, in the aggregate, beneficially own approximately 55.3% of our outstanding common stock. As a result, these persons, acting together, can significantly influence all matters requiring stockholder approval, including the election and removal of directors, any merger, consolidation, sale of all or substantially all of our assets, or other significant corporate transactions.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the current market price of our common stock and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders.

We are at risk of securities class action and similar litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of our securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. We remain the subject of various securities class action lawsuits and shareholder derivative lawsuits that were filed against OvaScience and certain of its officer and directors, as described in more detail in Item 3, Legal Proceedings. These lawsuits, as well as any similar lawsuits initiated in the future, could result in substantial cost and a diversion of management's attention and resources, which could harm our business.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Sarbanes-Oxley Act and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting and that we furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment includes disclosure of any material weaknesses identified by our management in our internal control over financial reporting. We are also required to have our auditors formally attest to the effectiveness of our internal control over financial reporting. For the year ended December 31, 2018, we were unable to conduct the required assessment primarily due to the Merger occurring in the fourth quarter of 2018 and the substantial change in operational focus, management and the internal control environment following the Merger. As a result, we are providing our first internal control assessment with this Annual Report as of December 31, 2019.

We may identify weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the Securities and Exchange Commission, or SEC, or other regulatory authorities.

We expect to continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to compliance with our public company responsibilities and corporate governance practices.

As a relatively new public company, we continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Capital Market and other applicable securities rules and regulations impose various requirements on public companies. Our management and other personnel need to devote a substantial amount of time to compliance with these requirements. Moreover, these rules and regulations increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain directors' and officers' liability insurance, compared to when we were a private company, which could make it more difficult for us to attract and retain qualified members of our board of directors. We cannot predict or estimate the amount of additional costs we will continue to incur as a public company or the timing of such costs.

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

On December 22, 2017, President Trump signed into law the Tax Act which 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 interest expense to 30% of adjusted earnings (except for certain small businesses), effective for net operating losses incurred in taxable years beginning after December 31, 2017, limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, 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 you to consult with your legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in more than one tax jurisdiction. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability from jurisdiction to jurisdiction, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

We might not be able to utilize a significant portion of our net operating loss carryforwards.

As of December 31, 2019, we had federal and state net operating loss carryforwards of $298.6 million and $262.5 million, respectively. The federal and state net operating loss carryforwards will begin to expire, if not utilized, by 2031. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain how various states will respond to the newly enacted federal tax law. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change has occurred or occurs in the future and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

We do not anticipate paying any cash dividends on our common stock in the foreseeable future.

You should not rely on an investment in our common stock to provide dividend income. We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of any existing or future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our corporate headquarters are located at 110 Miller Avenue, Suite 100, Ann Arbor, Michigan, 48104, where we occupy approximately 21,000 square feet of office space under two separate leases. We lease approximately 10,000 square feet of third floor office space pursuant to a lease entered into in October 2018, which began on July 1, 2019 and is set to expire on June 30, 2024. In addition, we lease approximately 11,000 square feet of first floor office space pursuant to a lease entered into in February 2019, which began on April 1, 2019 and is set to expire on March 31, 2024.

We also maintain approximately 4,058 square feet of flexible working space located at 420 Bedford Street, Lexington, Massachusetts, pursuant to a lease entered into in April 2019, which began on April 15, 2019 and ends on September 30, 2020.

We believe our existing facilities meet our current needs. We will need additional space in the future as we continue to build our development, commercial, and support teams.

ITEM 3. LEGAL PROCEEDINGS

Item 3. Legal Proceedings

On November 9, 2016, a purported shareholder derivative action was filed in the Business Litigation Session of the Suffolk County Superior Court in the Commonwealth of Massachusetts (*Cima v. Dipp*, No. 16-3443-BLS1 (Mass. Sup. Ct.)) against certain former officers and directors of OvaScience and one current director of the Company (a former director of OvaScience) and OvaScience as a nominal defendant alleging breaches of fiduciary duty, unjust enrichment, abuse of control, gross mismanagement and corporate waste for purported actions related to OvaScience's January 2015 follow-on public offering. On February 22, 2017, the court approved the parties' joint stipulation to stay all proceedings in the action until further notice. Following a status conference in December 2017, the stay was lifted. On January 25, 2018, at the parties' request, the court entered a second order staying all proceedings in the action until further order of the court. On March 2, 2020, the parties submitted a status report requesting that the Court continue the stay. We believe that the complaint is without merit and intend to defend against the litigation. There can be no assurance, however, that we will be successful. At present, we are unable to estimate potential losses, if any, related to the lawsuit.

On March 24, 2017, a purported shareholder class action lawsuit was filed in the U.S. District Court for the District of Massachusetts (*Dahhan v. OvaScience, Inc.*, No. 1:17-cv-10511-IT (D. Mass.)) against OvaScience and certain former officers and directors of OvaScience alleging violations of Sections 10(b) and 20(a) of the Exchange Act (the "Dahhan Action"). On July 5, 2017, the court entered an order approving the appointment of Freedman Family Investments LLC as lead plaintiff, the firm of Robins Geller Rudman & Dowd LLP as lead counsel and the Law Office of Alan L. Kovacs as local counsel. Plaintiff filed an amended complaint on August 25, 2017. We filed a motion to dismiss the amended complaint, which the court denied on July 31, 2018. On August 14, 2018, we answered the amended complaint. On December 9, 2019, the Court granted leave for plaintiff to file a second amended complaint under seal and permitted defendants to file a motion to strike the second amended complaint. On December 30, 2019, the Court granted the parties' joint motion to stay all proceedings in the case pending mediation. On March 3, 2020, the parties conducted a mediation session. As the mediation was unsuccessful, the parties are resuming discovery. We believe that the amended complaint and the second amended complaint are without merit and intend to defend against the litigation. There can be no assurance, however, that we will be successful. A resolution of this lawsuit adverse to the Company or the other defendants could have a material effect on the Company's consolidated financial position and results of operations. At present, we are unable to estimate potential losses, if any, related to the lawsuit.

On July 27, 2017, a purported shareholder derivative complaint was filed in the U.S. District Court for the District of Massachusetts (*Chiu v. Dipp*, No. 1:17-cv-11382-IT (D. Mass.)) against OvaScience, as a nominal defendant, certain former officers and directors of OvaScience and one current director of the Company (a former director of OvaScience) alleging breach of fiduciary duty, unjust enrichment and violations of Section 14(a) of the Exchange Act alleging that compensation awarded to the director defendants was excessive and seeking redress for purported actions related to OvaScience's January 2015 follow-on public offering and other public statements. On September 26, 2017, the plaintiff filed an amended complaint which eliminated all claims regarding allegedly excessive director pay and additionally alleged claims of abuse of control and corporate waste. On October 27, 2017, the defendants filed a motion to dismiss the amended complaint. The court heard oral argument on the motion to dismiss on April 5, 2018. On April 13, 2018, the court granted the defendants' motion to dismiss the amended complaint for failure to state a claim for relief under Section 14(a). The court also dismissed the plaintiffs' pendent state law claims without prejudice, based on lack of subject matter jurisdiction. On April 25, 2018, the plaintiffs moved for leave to amend the complaint, and to stay this case pending the outcome of the Dahhan Action. We do not believe that the proposed amended complaint cures the defects in the current complaint, but informed plaintiffs' counsel that, in the interest of judicial economy, defendants would not oppose the proposed amendment if the court would consider staying the case pending the resolution of the Dahhan Action. On April 27, 2018, the court granted the plaintiffs' motion for leave to amend the complaint and for a stay. On April 30, 2018, the plaintiffs filed their second amended complaint. On May 23, 2018, the court entered an order staying this case pending the resolution of the Dahhan Action. We believe that the complaint is without merit and intend to defend against the litigation. There can be no assurance, however, that we will be successful. At present, we are unable to estimate potential losses, if any, related to the lawsuit.

In addition to the matters described above, we may be a party to litigation and subject to claims incident to the ordinary course of business from time to time. Regardless of the outcome, litigation can have an adverse impact on the Company because of defense and settlement costs, diversion of management resources and other factors.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASE OF EQUITY SECURITIES

Market Information

Our common stock has been traded on the Nasdaq Global Market under the symbol "MLND" since the closing of the Merger on December 7, 2018.

Stockholders

As of March 1, 2020, we had 18,266,545 shares of common stock outstanding held by 86 holders of record. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

ITEM 6. SELECTED FINANCIAL DATA

Not required for smaller reporting companies.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the financial statements and the related notes to those statements included later in this Annual Report. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates, beliefs and expectations that involve risks and uncertainties. Our actual results and the timing of events could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report, particularly in Item 1A. "Risk Factors" and "Special Note Regarding Forward-Looking Statements."

Overview

We are a late-stage biopharmaceutical company primarily focused on developing novel treatments for orphan endocrine diseases where current therapies do not exist or are insufficient. The endocrine system is a collection of glands that secrete hormones into the blood stream to regulate a number of functions, including appetite, metabolism, growth, development and reproduction. Diseases of the endocrine system can cause multiple and varied symptoms, including appetite dysregulation, metabolic dysfunction, obesity, cardiovascular disease, menstrual irregularity, hirsutism, and infertility.

We are currently advancing three product candidates. Our most advanced product candidate, livoletide (AZP-531), is a potential treatment for Prader-Willi syndrome ("PWS"), a rare and complex genetic endocrine disease usually characterized by hyperphagia, or insatiable hunger, that contributes to serious complications, a significant burden on patients and caregivers, and early mortality. In a randomized, double-blind, placebo-controlled Phase 2a clinical trial in 47 patients with PWS, we observed that administration of livoletide once daily was associated with a clinically meaningful improvement in hyperphagia, as well as a reduction in appetite. In a pre-specified analysis of 38 home-resident patients with PWS from the Phase 2a trial, we observed a larger and statistically significant decrease in hyperphagia following administration of livoletide as compared to placebo. In March 2019, we initiated a Phase 2b/3 clinical trial of livoletide for the treatment of hyperphagia in patients with PWS. The randomized, double-blind, placebo-controlled pivotal Phase 2b trial includes 158 patients with PWS ages 8 to 65, recruited across 38 sites in the United States, Europe and Australia. As of February 26, 2020, the three-month "core" period of the Phase 2b trial has been completed. Topline results from the pivotal Phase 2b trial are expected in early second quarter of 2020. A

protocol amendment was submitted to the U.S. Food and Drug Administration, or FDA, on August 7, 2019, which allows 4- to 7-year-olds to participate in the Phase 2b/3 clinical trial. We continue to recruit patients in this age group. On July 29, 2019, the FDA designated the investigation of livoletide for PWS as a Fast Track development program. We are also conducting preclinical activities in support of the development of a multi-dose pen device to improve patient and caregiver convenience, as well as patient compliance, and to further simplify the administration of livoletide.

We are developing nevanimibe (ATR-101) as a potential treatment for patients with congenital adrenal hyperplasia ("CAH"), a rare, monogenic adrenal disease that requires lifelong treatment with exogenous cortisol, often at high doses. These chronic high doses of cortisol can result in side effects that include diabetes, obesity, hypertension and psychological problems. When on suboptimal doses of cortisol, female patients with CAH can experience hirsutism, infertility and menstrual irregularity, and male patients with CAH can experience testicular atrophy, infertility and testicular tumors. It is often difficult for physicians to appropriately treat CAH without causing adverse consequences. We reported results from our Phase 2a clinical trial of nevanimibe in patients with CAH in March 2018 and initiated a Phase 2b trial in the third quarter of 2018. We expect to report topline results from the first cohort of the Phase 2b trial in the second half of 2020. Enrollment for the second cohort of the Phase 2b trial is continuing and sites are actively enrolling patients. We expect to provide an additional update on the second cohort in the second half of 2020.

We also have a neurokinin 3 receptor (NK3R) antagonist (MLE-301) in our research and development pipeline, which we plan to develop as a potential treatment of vasomotor symptoms ("VMS"), commonly known as hot flashes and night sweats, in menopausal women. MLE-301 is currently in preclinical studies designed to enable first-in-human clinical studies, which we expect to initiate in the second half of 2020.

We had also been investigating nevanimibe (ATR-101) as a potential treatment for patients with endogenous Cushing's syndrome ("CS"), a rare endocrine disease characterized by excessive cortisol production from the adrenal glands. As a result of slower than anticipated enrollment in our CS Phase 2 clinical trial, we elected to discontinue the trial in August 2019, suspend development of nevanimibe for the treatment of CS, and focus our resources on other programs in our research and development pipeline.

Since our inception in January 2012, our operations have focused on conducting preclinical studies and clinical trials, acquiring technology and assets, organization and staffing, business planning, and raising capital. We have devoted substantial effort and resources to acquiring our three current product candidates, livoletide, nevanimibe, and MLE-301, as well as our previous product candidate, MLE4901, which we ceased developing in 2017. We acquired livoletide in connection with our acquisition of Alizé Pharma SAS, or Alizé, in December 2017. We in-licensed nevanimibe from the Regents of the University of Michigan, or the University of Michigan, in June 2013. We licensed MLE-301 from F. Hoffmann-La Roche Ltd and Hoffman-La Roche Inc. (collectively, "Roche"), in October 2018. We do not have any product candidates approved for sale and have not generated any revenue from product sales. We have funded our operations primarily through the sale and issuance of common stock, preferred stock and convertible promissory notes, proceeds received from the Merger as well as borrowings under term loans.

Since inception, we have incurred significant operating losses and negative operating cash flows and there is no assurance that we will ever achieve or sustain profitability. Our net losses were $44.6 million and $27.2 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $208.7 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase significantly in connection with our ongoing activities, including:

- continuing the ongoing and planned clinical development of livoletide and nevanimibe;
- continuing the preclinical development and potential clinical development of MLE-301;
- initiating preclinical studies and clinical trials for any additional diseases for our current product candidates and any future product candidates that we may pursue;
- building a portfolio of product candidates through the acquisition or in-license of drugs or product candidates and technologies;
- developing, maintaining, expanding and protecting our intellectual property portfolio;
- manufacturing, or having manufactured, clinical and commercial supplies of our product candidates;
- seeking marketing approvals for our current and future product candidates that successfully complete clinical trials;

- establishing a sales, marketing and distribution infrastructure to commercialize any product candidate for which we may obtain marketing approval;
- hiring additional administrative, clinical, regulatory and scientific personnel; and
- continuing to incur additional costs associated with operating as a public company.

Recent Events

Financing

In December 2019, we sold 4,791,667 shares of our common stock pursuant to an underwriting agreement (the "Underwriting Agreement") with Citigroup Global Markets Inc. and SVB Leerink LLC, as representatives of the several underwriters named therein (the "Underwriters"), for net proceeds to us of approximately $26.5 million, after deducting underwriting discounts and commissions and other offering expenses payable by us. The price to the public in this offering was $6.00 per share and resulted in the sale of 4,166,667 shares of our common stock for net proceeds to us of approximately $23.0 million, after deducting underwriting discounts and commissions and other offering expenses. In addition, the Underwriters purchased an additional 625,000 shares of our common stock at the public offering price of $6.00 per share pursuant to a purchase option granted to them under the Underwriting Agreement, resulting in net proceeds to us of approximately $3.5 million, after deducting underwriting discounts and commissions.

The offering was made pursuant to our registration statement on Form S-3 (Registration Statement No. 333-230749), which was declared effective by the Securities and Exchange Commission on April 18, 2019, and a prospectus supplement thereunder.

At-the-Market Equity Distribution Agreement

In April 2019, we entered into an "at-the-market" ("ATM") equity distribution agreement with Citigroup Global Markets Inc. acting as sole agent with an aggregate offering value of up to $50.0 million which allows us to sell our common stock through the facilities of the Nasdaq Capital Market. Subject to the terms of the equity distribution agreement, we are able to determine, at our sole discretion, the timing and number of shares to be sold under this ATM facility. In March 2020, we amended the equity distribution agreement to include SVB Leerink LLC as an additional sales agent for the ATM. In March 2020, we sold 719,400 shares of our common stock under our ATM equity distribution agreement for estimated net proceeds to us of approximately $5.5 million.

Sales of our common stock pursuant to the ATM have been made pursuant to our registration statement on Form S-3 (Registration Statement No. 333-230749), which was declared effective by the Securities and Exchange Commission on April 18, 2019.

Merger

On December 7, 2018, OvaScience, Inc., or OvaScience, now known as Millendo Therapeutics, Inc. completed its reverse merger or, the Merger, with what was then known as "Millendo Therapeutics, Inc.," or Private Millendo, in accordance with the terms of the Agreement and Plan of Merger and Reorganization dated as of August 8, 2018, as amended on September 25, 2018 and November 1, 2018, or the Merger Agreement. OvaScience's shares of common stock listed on The Nasdaq Capital Market, previously trading through the close of business on Friday, December 7, 2018 under the ticker symbol "OVAS," commenced trading on The Nasdaq Capital Market, under the ticker symbol "MLND," on Monday, December 10, 2018.

In August 2018, Private Millendo issued convertible promissory notes, or the Notes, to several of its existing investors and received cash proceeds of $8.0 million. The Notes accrued simple interest of 6.0% per annum. Additionally, immediately prior to the Merger, Private Millendo issued and sold an aggregate of 1,320,129 shares of Private Millendo common stock for total net proceeds of approximately $20.1 million, or the Pre-Closing Financing, to certain existing stockholders of Private Millendo.

In connection with the Merger, each outstanding share of Private Millendo capital stock converted into shares of OvaScience's common stock, and each outstanding option or warrant to purchase Private Millendo capital stock converted into the right to receive shares of OvaScience's common stock. At the Closing of the Merger, Private Millendo stockholders received an aggregate of 8,789,628 shares of OvaScience common stock, which includes 1,320,129 shares of common stock issued to the investors in the Pre-Closing Financing, Private Millendo option holders received options to purchase 1,874,158 shares of OvaScience common stock and Private Millendo warrant holders received warrants to purchase 17,125 shares of OvaScience

common stock. In addition, upon the Closing of the Merger, all principal and interest underlying the Notes converted into 499,504 shares of OvaScience common stock.

Immediately following the Merger, Private Millendo became a wholly-owned subsidiary of OvaScience. Upon consummation of the Merger, or the Closing, OvaScience adopted the business plan of Private Millendo and discontinued the pursuit of OvaScience's business plan pre-Closing. The Merger was accounted for as a reverse recapitalization with Private Millendo as the accounting acquirer. On the Merger date, the primary pre-combination assets of OvaScience was cash, cash equivalents and marketable securities. At the time of the Merger, OvaScience had net assets of $38.0 million, which was comprised primarily of cash, cash equivalents and marketable securities. See Note 3 of our Consolidated Financial Statements for additional information regarding the Merger accounting treatment.

Following the Closing of the Merger, on December 7, 2018, we issued and sold an aggregate of 1,230,158 shares of common stock to an institutional investor for $16.258065 per share, for total net proceeds of approximately $18.7 million.

Integration of OvaScience

Leading up to the closing date of the Merger, OvaScience had agreed to terminate, assign or otherwise fully discharge substantially all obligations under all contracts to which OvaScience or its subsidiaries were a party, wind-down the operations, and dissolve certain subsidiaries. OvaScience has closed their offices and all employees were terminated or resigned prior to or at the closing. All operations are drawing to a close that were not already wound down prior to closing.

Acquisition of Alizé

In December 2017, Private Millendo entered into agreements to acquire 100% of the outstanding ownership interests of Alizé, a privately held biotechnology company based in Lyon, France focused on the development of a treatment for patients with PWS, through its lead product candidate, livoletide.

In December 2017, we acquired 83.6% of the issued and outstanding share capital of Alizé pursuant to a Share Sale and Contribution Agreement. The consideration included an upfront payment of $1.0 million, and the issuance of Private Millendo's Series A-1 preferred stock, Series B-1 preferred stock, and common-1 stock, which upon consummation of the Merger were converted to shares of our common stock. In December 2018, we acquired the remaining 16.4% of Alizé's issued and outstanding share capital from Otonnale SAS, or Otonnale. The consideration included a cash payment of $0.8 million and the issuance of the 442,470 shares of our common stock.

The Share and Contribution Agreement with Alizé was accounted for as an asset acquisition as substantially all of the fair value of the gross assets acquired was concentrated in the livoletide development program. The $63.8 million in estimated fair value allocated to livoletide was expensed, as we determined the asset has no alternative future use. The total consideration given, net of cash acquired was $63.1 million. The assets acquired and liabilities assumed as of the acquisition date were $65.3 million and $2.2 million, respectively, for net assets acquired of $63.1 million.

Components of Results of Operations

Research and development expense

Research and development expense consists primarily of costs incurred in connection with the development of our product candidates. We expense research and development costs as incurred. These expenses include:

- personnel expenses, including salaries, benefits and stock-based compensation expense;
- costs of funding research performed by third parties, including pursuant to agreements with contract research organizations ("CROs"), as well as investigative sites and consultants that conduct our preclinical studies and clinical trials;
- expenses incurred under agreements with contract manufacturing organizations ("CMOs"), including manufacturing scale-up expenses and the cost of acquiring and manufacturing preclinical study and clinical trial materials;
- payments made under our third-party licensing agreements;
- consultant fees and expenses associated with outsourced professional scientific development services;

- expenses for regulatory activities, including filing fees paid to regulatory agencies; and
- allocated expenses for facility costs, including rent, utilities, depreciation and maintenance.

Milestone payment obligations incurred prior to regulatory approval of a product candidate, which are accrued when the event requiring payment of the milestone occurs are included in research and development expense.

We typically use our employee, consultant and infrastructure resources across our development programs. We track certain outsourced development costs by product candidate, but do not allocate all personnel costs or other internal costs to specific product candidates.

The following table summarizes our research and development expenses by product candidate, personnel expense and other expenses for the years ended December 31, 2019 and 2018, respectively:

	Year Ended December 31,	
	2019	2018
	(in thousands)	
Livoletide expenses	$ 14,702	$ 4,921
Nevanimibe expenses	2,899	4,108
MLE-301 expenses	2,723	—
Personnel expenses	6,559	4,616
Other expenses	960	780
Total	$ 27,843	$ 14,425

We expect our research and development expense will increase for the foreseeable future as we seek to advance development of our product candidates. The successful development of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the remainder of the development of livoletide, nevanimibe, or MLE-301. We are also unable to predict when, if ever, material net cash inflows may commence from sales of livoletide, nevanimibe, MLE-301 or any future product candidates that we may develop due to the numerous risks and uncertainties associated with clinical development, including risks and uncertainties related to:

- the number of clinical sites included in the trials;
- the length of time required to enroll suitable patients;
- the number of patients that ultimately participate in the trials;
- the number of doses patients receive;
- the duration of patient follow-up and number of patient visits;
- the results of our clinical trials;
- the establishment of commercial manufacturing capabilities;
- the receipt of marketing approvals; and
- the commercialization of product candidates.

We may never succeed in obtaining regulatory approval for livoletide, nevanimibe, MLE-301 or any future product candidates we may develop. Product candidates in later stages of clinical development, like livoletide and nevanimibe, generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials.

General and administrative expense

General and administrative expense consists primarily of personnel expenses, including salaries, benefits and stock-based compensation expense, for employees in executive, finance, accounting, business development, legal and human resource functions. General and administrative expense also includes corporate facility costs, including rent, utilities, depreciation and

maintenance, not otherwise included in research and development expense, as well as legal fees related to intellectual property and corporate matters and fees for accounting, recruiting and consulting services.

We anticipate that our general and administrative expense will increase as we support additional clinical trials for livoletide, nevanimibe and MLE-301. In addition, if and when we believe that regulatory approval of livoletide, nevanimibe or MLE-301 appears likely, we anticipate an increase in headcount and related expense as a result of our preparation for commercial operations.

Other general expenses

Other general expenses consist of professional fees and severance costs incurred in connection with the Merger in 2018.

Interest expense (income), net

Interest expense (income) represents amounts earned on our cash, cash equivalents, marketable securities and restricted cash balances.

Change in fair value of preferred stock warrant liability

Change in fair value of preferred stock warrant liability reflects the change in the fair value of our outstanding preferred stock warrants, which is primarily driven by changes in the fair value of the underlying preferred stock. Outstanding warrants to purchase shares of our preferred stock were classified as liabilities and were subject to re-measurement at each balance sheet date until consummation of the Merger whereby the warrants were exchanged for warrants to receive shares of our common stock. Upon completing the exchange, the warrants were eligible for equity classification and no longer subject to re-measurement.

Results of operations

Comparison of the years ended December 31, 2019 and 2018

	Year Ended December 31,	
	2019	2018
	(in thousands)	
Operating expenses:		
Research and development	$ 27,843	$ 14,425
General and administrative	17,556	8,691
Other general expenses	—	3,758
Loss from operations	45,399	26,874
Other expenses:		
Interest expense (income), net	(1,038)	134
Other loss	207	169
Net loss	$ 44,568	$ 27,177

Research and development expense

Research and development expense increased by $13.4 million to $27.8 million for the year ended December 31, 2019 from $14.4 million for the year ended December 31, 2018. The following table summarizes our research and development expenses for the years ended December 31, 2019 and 2018:

	Year Ended December 31,	
	2019	2018
	(in thousands)	
Preclinical and clinical development expense	$ 20,324	$ 9,272
Compensation expense, other than stock-based compensation	5,260	4,010
Stock-based compensation expense	1,299	606
Other expenses	960	537
Total research and development expense	$ 27,843	$ 14,425

The increase in total research and development expense is attributable to:

- a $11.1 million increase in preclinical and clinical development expense mainly related to the development of livoletide;
- a $1.9 million increase in compensation and stock-based compensation expenses as a result of our increase in research and development headcount and additional options granted; and
- a $0.4 million increase in other expenses mainly related to the development of livoletide due to allocated rent and facility costs.

General and administrative expense

General and administrative expense increased by $8.9 million to $17.6 million for the year ended December 31, 2019 from $8.7 million for the year ended December 31, 2018. The increase was primarily due to a $4.3 million increase in compensation and stock-based compensation expense as a result of our increase in general and administrative headcount and changes to compensation arrangements, a $2.6 million increase in professional fees incurred mainly related to being a publicly traded company, and a $1.9 million increase in insurance, rent and facility related. The increase in insurance is due to operating as a public company and the increase in rent and facility related expenses is due to increased headcount and additional leased office space.

Other general expenses

In connection with the Merger in 2018, we incurred $3.8 million of transaction related costs mainly due to professional fees and severance.

Interest expense (income), net

Interest expense (income), net increased by $1.2 million to $1.0 million net interest income for the year ended December 31, 2019 from $0.1 million net interest expense for the year ended December 31, 2018. The change was primarily due to higher interest income received as a result of larger cash, cash equivalent, restricted cash, and marketable securities balances we had immediately following the Merger.

Other loss

Other loss increased by $38,000 to $207,000 for the year ended December 31, 2019 from $169,000 for the year ended December 31, 2018. The increase was due to higher foreign currency losses as a result of exchange rate fluctuations on transactions denominated in a currency other than our functional currency.

Liquidity and Capital Resources

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

	Year Ended December 31,	
	2019	2018
	(in thousands)	
Net cash used in operating activities	$ (41,222)	$ (23,647)
Net cash provided by investing activities	3,988	1,932
Net cash provided by financing activities	26,943	77,744
Effect of foreign currency exchange rate changes on cash	33	118
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (10,258)	$ 56,147

Uses of funds

Operating activities

During the year ended December 31, 2019, we used $41.2 million of cash to fund operating activities. During the year ended December 31, 2019, cash used in operating activities reflected our net loss of $44.6 million and a net change in operating assets and liabilities of $2.0 million, offset by non-cash charges of $5.4 million, principally related to stock-based compensation.

During the year ended December 31, 2018, we used $23.6 million of cash in operating activities. Cash used in operating activities reflected our net loss of $27.2 million, offset by a net increase in operating assets and liabilities of $1.1 million and non-cash charges of $2.5 million, principally related to stock-based compensation, write-off of deferred financing costs, non-cash interest and changes in fair value of our preferred stock warrant liability.

Investing activities

During the year ended December 31, 2019, we received $4.4 million in net proceeds from the sale of marketable securities offset by $0.4 million in purchases of property and equipment.

During the year ended December 31, 2018, we received $2.5 million in net proceeds from the sale of marketable securities and paid $0.5 million in acquisition costs previously accrued in connection with the asset acquisition of Alizé.

Financing activities

During the year ended December 31, 2019, we received proceeds of $0.5 million from the exercise of options and warrants, and $26.7 million in proceeds received from the issuance of common stock, net of issuance costs paid. See Note 1 of our Consolidated Financial Statements for additional information related to the issuance of common stock. These proceeds were offset by $0.2 million for the repayment of debt.

During the year ended December 31, 2018, financing activities provided $77.7 million in net cash, primarily attributable to cash acquired in connection with the Merger of $33.3 million and $38.8 million in net proceeds from the sale of our common stock in private placements of which $20.1 million was received prior to the Merger and $18.7 million was received immediately following the consummation of the Merger. We also received $8.0 million in proceeds from the issuance of convertible promissory notes in August 2018 that were converted into shares of our common stock in December 2018 upon consummation of the Merger. These cash inflows were offset by payments of $1.4 million in related financing costs, payment of $0.8 million in connection with the repurchase of redeemable non-controlling interests, and repayments of $0.2 million of debt.

Funding requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, continue or initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we in the future submit an NDA in the United States or a marketing authorization application in Europe for any of our product candidates, we expect to incur significant costs in connection with the submission as well as significant commercialization expenses related to program sales, marketing, manufacturing and distribution, which expenses we expect to incur prior to generating any revenues from product sales. Accordingly, we will need to obtain substantial additional funding in connection

with our current and future operations. If we are unable to raise capital when needed or on attractive terms, we may would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

In April 2019, we entered into an "at-the-market" ("ATM") equity distribution agreement with Citigroup Global Markets Inc. acting as sole agent with an aggregate offering value of up to $50.0 million which allows us to sell our common stock through the facilities of the Nasdaq Capital Market. Subject to the terms of the equity distribution agreement, we are able to determine, at our sole discretion, the timing and number of shares to be sold under this ATM facility. In March 2020, we amended the equity distribution agreement to include SVB Leerink LLC as an additional sales agent for the ATM. In March 2020, we sold 719,400 shares of our common stock under our ATM equity distribution agreement for estimated net proceeds to us of approximately $5.5 million.

As of December 31, 2019, we had cash, cash equivalents, marketable securities and restricted cash of $63.5 million, which, in addition to funds received in connection with shares issued under the ATM equity distribution agreement in March 2020, we believe are sufficient to fund our planned operations into 2022. This cash runway guidance is based on our current operational plans and excludes any additional funding that may be received and business development or commercialization activities that may be undertaken. In addition, our operating plans may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, third-party funding, and marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. In any event, we will require additional capital to pursue regulatory approval and the commercialization of our current and future product candidates.

Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of preclinical studies and clinical trials;
- the scope, prioritization and number of our research and development programs;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under collaboration agreements, if any;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire or in-license other product candidates and technologies;
- the costs of securing manufacturing arrangements for commercial production; and
- the costs of establishing or contracting for sales and marketing capabilities if we obtain regulatory approvals to market our product candidates.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of product candidates that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. 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.

If we raise funds through additional 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 future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

The following table summarizes our commitments to settle contractual obligations at December 31, 2019:

	Year Ended December 31 2019,				
	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years	Total
	(in thousands)				
Operating leases [1]	$ 1,803	$ 1,633	$ 1,198	$ 45	$ 4,679
Long-term debt [2]	208	168	—	—	376
Licensing arrangements [3]	20	60	—	— [4]	80 [4]
Total	$ 2,031	$ 1,861	$ 1,198	$ 45 [4]	$ 5,135 [4]

(1) Reflects obligations pursuant to our office leases in Ann Arbor, Michigan; Waltham, Massachusetts; Lexington Massachusetts; and Lyon, France. In January 2020, we terminated our office lease agreement in Lyon, France.

(2) Reflects obligations pursuant to our advance agreement with Bpifrance Financing. In December 2017, in connection with our acquisition of Alizé, we assumed €0.7 million of debt that Alizé had outstanding with Bpifrance Financing. No interest is charged or accrued with respect to the debt. We are required to make quarterly principal payments between €17,500 to €50,000 per quarter through maturity. In addition to the quarterly payments, we could be obligated to pay, if applicable, no later than March 31 of each year starting from January 1, 2016, a reimbursement annuity equal to 20% of the proceeds generated by us from license, assignment or revenue-generating use of the livoletide program. We are permitted to repay the debt at any time.

(3) Reflects obligations pursuant to our license agreements with the University of Michigan, other than contingent obligations to make milestone and royalty payments where the amount, likelihood and timing of such payments are not fixed or determinable. Contingent payments pursuant to our license agreements with Erasmus University Medical Center and Roche are also excluded from the above table.

(4) We are obligated to pay the University of Michigan minimum royalties of $20,000 per year from 2020 to 2023 and $0.2 million per year beginning in 2024 through expiration of the term of the license agreement. All such amounts due after December 31, 2023 are excluded from the table above because the duration of the license agreement is not determinable.

The commitment amounts in the table above are associated with contracts that are enforceable and legally binding and that specify all significant terms, including fixed or minimum services to be used, fixed, minimum or variable price provisions, and the approximate timing of the actions under the contracts. The table does not include obligations under agreements that we can cancel without a significant penalty.

Off-Balance Sheet Arrangements

We do not have any relationships with unconsolidated entities or financial partnerships, including entities sometimes referred to as structured finance or special purpose entities that were established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purposes. We do not engage in off-balance sheet financing arrangements. In addition, we do not engage in trading activities involving non-exchange traded contracts. We therefore believe that we are not materially exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in these relationships.

Critical Accounting Policies

Our Consolidated Financial Statements are prepared in accordance with U.S. GAAP. The preparation of our Consolidated Financial Statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the Consolidated Financial Statements and the reported amounts of

expenses during the reported period. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions and conditions.

Research and development expenses

Research and development expense consists primarily of costs incurred in connection with the development of our product candidates. We expense research and development costs as incurred.

At the end of each reporting period, we compare payments made to third-party service providers to the estimated progress toward completion of the applicable research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the progress that we estimate has been made as a result of the service provided, we may record net prepaid or accrued expense relating to these costs. As of December 31, 2019, we had not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-based compensation

We measure expense for all stock options based on the estimated fair market value of the award on the grant date. We use the Black-Scholes option pricing model to value our stock option awards. We recognize compensation expense on a straight-line basis over the requisite service period, which is generally the vesting period of the award. We have not issued awards where vesting is subject to a market or performance condition; however, if we were to grant such awards in the future, recognition would be based on the derived service period. Expense for awards with performance conditions would be estimated and adjusted on a quarterly basis based upon our assessment of the probability that the performance condition will be met.

Historically, for all periods prior to the Merger, the fair market values of the shares of common stock underlying our stock options were estimated on each grant date by the board of directors. In order to determine the fair market value of our common stock, our board of directors considered, among other things, contemporaneous valuations of our common and preferred stock prepared by unrelated third-party valuation firms in accordance with the guidance provided by the American Institute of Certified Public Accountants 2013 Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or Practice Aid. Given the absence of a public trading market of our capital stock, the our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair market value of our common and preferred stock, including:

- contemporaneous third-party valuations of our common stock;
- the prices, rights, preferences and privileges of our preferred stock relative to the common stock;
- our business, financial condition and results of operations, including related industry trends affecting our operations;
- the likelihood of achieving a liquidity event, such as an IPO or sale of our company, given prevailing market conditions;
- the lack of marketability of our common stock;
- the market performance of comparable publicly traded companies; and
- U.S. and global economic and capital market conditions and outlook.

Following the Merger, the fair market value of our common stock was determined based on the closing price of our common stock on the Nasdaq Capital Market.

Recent Accounting Pronouncements

See Note 2 to our Consolidated Financial Statements for a description of recent accounting pronouncements applicable to its Consolidated Financial Statements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Not required for smaller reporting companies.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

MILLENDO THERAPEUTICS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Millendo Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Millendo Therapeutics, Inc. (the Company) as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, convertible preferred stock, redeemable noncontrolling interests and stockholders' (deficit) equity, and cash flows for each of the two years in the period ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 11, 2020 expressed an unqualified opinion thereon.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2016.
Grand Rapids, Michigan
March 11, 2020

Millendo Therapeutics, Inc.

Consolidated Balance Sheets

(in thousands except share and per share amounts)

	December 31,	
	2019	2018
Assets		
Current assets:		
Cash and cash equivalents	$ 62,478	$ 73,286
Short-term restricted cash	1,034	45
Marketable securities	—	4,385
Prepaid expenses and other current assets	6,344	3,373
Refundable tax credit	1,276	2,333
Total current assets	71,132	83,422
Long-term restricted cash	—	439
Operating lease right-of-use assets	3,331	—
Other assets	507	213
Total assets	$ 74,970	$ 84,074
Liabilities and stockholders' equity		
Current liabilities:		
Current portion of debt	$ 208	$ 189
Accounts payable	1,495	1,998
Accrued expenses	9,066	7,630
Operating lease liabilities - current	1,751	—
Total current liabilities	12,520	9,817
Debt, net of current portion	168	383
Operating lease liabilities	2,395	—
Other liabilities	16	752
Total liabilities	15,099	10,952
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value: 5,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.001 par value: 100,000,000 shares authorized; 18,266,545 shares and 13,357,999 shares issued and outstanding at December 31, 2019 and 2018, respectively	18	13
Additional paid-in capital	267,018	234,876
Accumulated deficit	(208,654)	(164,086)
Accumulated other comprehensive income	165	148
Total stockholders' equity attributable to Millendo Therapeutics, Inc.	58,547	70,951
Equity attributable to noncontrolling interests	1,324	2,171
Total stockholders' equity	59,871	73,122
Total liabilities and stockholders' equity	$ 74,970	$ 84,074

See accompanying Notes to Consolidated Financial Statements

Millendo Therapeutics, Inc.

Consolidated Statements of Operations and Comprehensive Loss

(in thousands except share and per share amounts)

	Year Ended December 31,	
	2019	**2018**
Operating expenses:		
Research and development	$ 27,843	$ 14,425
General and administrative	17,556	8,691
Other general expenses	—	3,758
Loss from operations	45,399	26,874
Other expenses:		
Interest expense (income), net	(1,038)	134
Other loss	207	169
Net loss	(44,568)	(27,177)
Net (income) loss attributable to noncontrolling interest	—	(15)
Net loss attributable to common stockholders	$ (44,568)	$ (27,192)
Net loss per share of common stock, basic and diluted	$ (3.25)	$ (17.58)
Weighted-average shares of common stock outstanding, basic and diluted	13,706,744	1,547,051
Other comprehensive income (loss):		
Foreign currency translation adjustment	$ 17	$ 140
Comprehensive loss	$ (44,551)	$ (27,052)

See accompanying Notes to Consolidated Financial Statements

Millendo Therapeutics, Inc.

Consolidated Statements of Convertible Preferred Stock, Redeemable Noncontrolling Interests and Stockholders' Equity (Deficit)

(in thousands except share amounts)

	Convertible Preferred Stock			Stockholders' Equity (Deficit)									
				Common Stock		Common-1 Stock							
	Shares	Amount	Redeemable Noncontrolling Interests	Shares	Amount	Shares	Amount	Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' (Deficit) attributable to Millendo Therapeutics, Inc.	Total Equity Attributable to Noncontrolling Interests	Total Stockholders' (Deficit) Equity
Balance at January 1, 2018	90,848,515	$ 132,922	$ 10,584	246,347	$ —	464,043	$ —	$ 6,192	$ (136,894)	$ 8	$ (130,694)	$ 2,171	$ (128,523)
Conversion of convertible preferred stock into common stock	(90,848,515)	(132,922)	—	6,759,109	7	—	—	132,915	—	—	132,922	—	132,922
Reclassification of preferred stock warrant liability	—	—	—	—	—	—	—	99	—	—	99	—	99
Conversion of common-1 stock into common stock	—	—	—	464,043	—	(464,043)	—	—	—	—	—	—	—
Conversion of convertible promissory note into common stock	—	—	—	499,504	1	—	—	7,723	—	—	7,724	—	7,724
Private placement of common stock (pre-Merger), net of issuance costs	—	—	—	1,320,129	1	—	—	20,053	—	—	20,054	—	20,054
Record pre-merger OvaScience stockholders' equity and elimination of OvaScience historical accumulated deficit	—	—	—	2,388,338	2	—	—	37,992	—	—	37,994	—	37,994
Private placement of common stock (post-Merger), net of issuance costs	—	—	—	1,230,158	1	—	—	18,686	—	—	18,687	—	18,687
Repurchase of redeemable noncontrolling interest	—	—	(10,599)	450,371	1	—	—	9,789	—	—	9,790	—	9,790
Stock-based compensation expense	—	—	—	—	—	—	—	1,427	—	—	1,427	—	1,427
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	140	140	—	140
Net income (loss)	—	—	15	—	—	—	—	—	(27,192)	—	(27,192)	—	(27,192)
Balance at December 31, 2018	—	$ —	$ —	13,357,999	$ 13	—	$ —	$ 234,876	$ (164,086)	$ 148	$ 70,951	$ 2,171	$ 73,122
Exercise of stock options	—	—	—	97,225	—	—	—	361	—	—	361	—	361
Issuance of common stock to board of directors	—	—	—	1,941	—	—	—	20	—	—	20	—	20
Issuance of common stock, net of issuance costs	—	—	—	4,791,667	5	—	—	26,486	—	—	26,491	—	26,491
Exercise/forfeiture of BSPCE warrants	—	—	—	17,713	—	—	—	958	—	—	958	(847)	111
Stock-based compensation expense	—	—	—	—	—	—	—	4,317	—	—	4,317	—	4,317
Foreign currency translation adjustment	—	—	—	—	—	—	—	—	—	17	17	—	17
Net income (loss)	—	—	—	—	—	—	—	—	(44,568)	—	(44,568)	—	(44,568)
Balance at December 31, 2019	—	$ —	$ —	18,266,545	$ 18	—	$ —	$ 267,018	$ (208,654)	$ 165	$ 58,547	$ 1,324	$ 59,871

See accompanying Notes to Consolidated Financial Statements

Millendo Therapeutics, Inc.

Consolidated Statements of Cash Flows

(in thousands)

	Year Ended December 31,	
	2019	**2018**
Operating activities:		
Net loss	$ (44,568)	$ (27,177)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	97	32
Stock-based compensation expense	4,317	1,427
Write-off of deferred financing costs	—	871
Non-cash interest	—	204
Amortization of right-of-use asset	955	—
Change in fair value of preferred stock warrant liability	—	(40)
Other non-cash items	30	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(698)	(2,524)
Other assets	66	—
Accounts payable	(469)	320
Accrued expenses and other liabilities	281	3,240
Operating lease liabilities	(1,233)	—
Cash used in operating activities	(41,222)	(23,647)
Investing activities:		
Purchase of property and equipment	(397)	(36)
Proceeds from sale of marketable securities	4,385	2,492
Net cash paid in Alizé asset purchase	—	(524)
Cash provided by investing activities	3,988	1,932
Financing activities:		
Cash acquired in connection with the Merger	—	33,316
Proceeds from convertible promissory notes	—	8,000
Repayment of debt and principal on finance lease	(202)	(169)
Proceeds from the issuance of common stock, net of issuance costs	26,688	—
Proceeds from sale of private placement, net of issuance costs	(15)	38,756
Payment of financing costs	—	(1,351)
Purchase of redeemable noncontrolling interest	—	(808)
Proceeds from option and BSPCE warrant exercises	472	—
Cash provided by financing activities	26,943	77,744
Effect of foreign currency exchange rate changes on cash	33	118
Net increase (decrease) in cash, cash equivalents and restricted cash	(10,258)	56,147
Cash, cash equivalents and restricted cash at beginning of period	73,770	17,623
Cash, cash equivalents and restricted cash at end of period	$ 63,512	$ 73,770
Supplemental disclosure of cash flow information:		
Cash paid for taxes	$ —	$ 4
Supplemental schedule of non-cash investing and financing activities:		
Conversion of convertible preferred stock into common stock	$ —	$ 132,922
Reclassification of preferred stock warrant liability	$ —	$ 99
Conversion of convertible promissory note into common stock	$ —	$ 7,724
Exchange of noncontrolling interest	$ —	$ 9,790
Financing costs in accounts payable and accrued expenses	$ 197	$ 15
Right-of-use assets acquired under operating leases	$ 3,414	$ —

See accompanying Notes to Consolidated Financial Statements

Millendo Therapeutics, Inc.

Notes to Consolidated Financial Statements

1. Organization and Description of Business

Description of Business

Millendo Therapeutics, Inc. (the "Company"), a Delaware corporation, together with its subsidiaries, is a late-stage biopharmaceutical company primarily focused on developing novel treatments for orphan endocrine diseases where current therapies do not exist or are insufficient. The Company is currently advancing three product candidates. The Company's most advanced product candidate, livoletide (AZP-531), is a potential treatment for Prader-Willi syndrome, ("PWS"), a rare and complex genetic endocrine disease usually characterized by hyperphagia, or insatiable hunger. The Company is also developing nevanimibe (ATR-101) as a potential treatment for patients with classic congenital adrenal hyperplasia, ("CAH"), a rare, monogenic adrenal disease that requires lifelong treatment with exogenous cortisol, often at high doses. The Company also has a neurokinin 3-receptor (NK3R) antagonist (MLE-301) in its research and development pipeline, which it plans to develop as a potential treatment of vasomotor symptoms ("VMS"), commonly known as hot flashes and night sweats, in menopausal women.

The Company had also been investigating nevanimibe (ATR-101) as a potential treatment for patients with endogenous Cushing's syndrome ("CS"), a rare endocrine disease characterized by excessive cortisol production from the adrenal glands. As a result of slower than anticipated enrollment in its CS Phase 2 clinical trial, the Company elected to discontinue this trial in August 2019, suspend development of nevanimibe for the treatment of CS, and focus its resources on other programs in its research and development pipeline.

The Company's operations to date have focused on conducting preclinical studies and clinical trials, acquiring technology and assets, organization and staffing, business planning, and raising capital. The Company does not have any products approved for sale and has not generated any revenue from product sales. The Company's product candidates are subject to long development cycles and the Company may be unsuccessful in its efforts to develop, obtain regulatory approval for or market its product candidates.

The Company is subject to a number of risks including, but not limited to, the need to obtain adequate additional funding for the ongoing and planned clinical development of its product candidates. Because of the numerous risks and uncertainties associated with pharmaceutical products and development, the Company is unable to accurately predict the timing or amount of funds required to complete development of its product candidates, and costs could exceed the Company's expectations for a number of reasons, including reasons beyond the Company's control.

Merger with OvaScience

In December 2018, OvaScience, Inc., a Delaware corporation ("OvaScience"), now known as Millendo Therapeutics, Inc., completed its merger (the "Merger") with privately-held Millendo Therapeutics, Inc. ("Private Millendo"), in accordance with the terms of the Agreement and Plan of Merger and Reorganization, dated August 8, 2018, as amended on September 25, 2018 and November 1, 2018 (the "Merger Agreement"), whereby Orion Merger Sub, Inc., a Delaware corporation and wholly-owned subsidiary of OvaScience (the "Merger Sub"), merged with and into Private Millendo, with Private Millendo continuing as a wholly owned subsidiary of OvaScience.

Under the terms of the Merger Agreement, OvaScience issued shares of its common stock to Private Millendo's stockholders, at an exchange ratio of 0.0744 shares of OvaScience common stock, for each share of Private Millendo common stock outstanding immediately prior to the Merger. OvaScience also assumed all of the stock options outstanding under the Private Millendo 2012 Equity Incentive Plan, as amended (the "Private Millendo Plan"), with such stock options henceforth representing the right to purchase a number of shares of OvaScience's common stock equal to 0.0744 multiplied by the number of shares of Private Millendo common stock previously represented by such options.

The Company's shares of common stock listed on the Nasdaq Capital Market, previously trading through the close of business on Friday, December 7, 2018 (the "Merger Date") under the ticker symbol "OVAS," commenced trading on the Nasdaq Capital Market, under the ticker symbol "MLND," on Monday, December 10, 2018. See discussions of the transactions in connection with the Merger within Note 3.

The Merger was accounted for as a reverse acquisition and recapitalization, with Private Millendo being treated as the accounting acquirer. As such, the results of operations and cash flows prior to the Merger Date, relate to Private Millendo and its subsidiaries. Subsequent to the Merger Date, the information relates to the consolidated entities of Millendo Therapeutics, Inc. All share and per share amounts in the Consolidated Financial Statements and related notes have been retroactively adjusted, where applicable, for all periods presented to give effect to the exchange ratio applied in connection with the Merger.

Acquisition of Alizé

In December 2017, the Company entered into agreements to acquire 100% of the outstanding ownership interests of Alizé, a privately held biotechnology company based in Lyon, France focused on the development of a treatment for patients with PWS, through its lead product candidate, livoletide.

In December 2017, the Company acquired 83.6% of the issued and outstanding share capital of Alizé pursuant to a Share Sale and Contribution Agreement. In December 2018, the Company acquired the remaining 16.4% of Alizé's issued and outstanding share capital from Otonnale SAS, or Otonnale.

Liquidity

The Company has incurred net losses since inception and it expects to generate losses from operations for the foreseeable future primarily due to research and development costs for its potential product candidates. As of December 31, 2019, the Company had cash, cash equivalents, marketable securities and restricted cash of $63.5 million and an accumulated deficit of $208.7 million.

In December 2019, the Company sold a total of 4,791,667 shares of its common stock pursuant to an underwriting agreement (the "Underwriting Agreement") with Citigroup Global Markets Inc. and SVB Leerink LLC, as representatives of the several underwriters named therein (the "Underwriters"), for total net proceeds of approximately $26.5 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company. The price to the public in this offering was $6.00 per share and resulted in the sale of 4,166,667 shares of the Company's common stock for net proceeds of approximately $23.0 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company. In addition, the Underwriters purchased an additional 625,000 shares of the Company's common stock at the public offering price of $6.00 per share pursuant to a purchase option granted to them under the Underwriting Agreement, resulting in net proceeds of approximately $3.5 million, after deducting underwriting discounts and commissions.

In April 2019, the Company entered into an "at-the-market" ("ATM") equity distribution agreement with Citigroup Global Markets Inc. acting as sole agent with an aggregate offering value of up to $50.0 million, which allows the Company to sell its common stock through the facilities of the Nasdaq Capital Market. Subject to the terms of the ATM equity distribution agreement, the Company is able to determine, at its sole discretion, the timing and number of shares to be sold under this ATM facility. In March 2020, the Company amended the equity distribution agreement to include SVB Leerink LLC as an additional sales agent for the ATM. In March 2020, we sold 719,400 shares of our common stock under our ATM equity distribution agreement for estimated net proceeds to us of approximately $5.5 million.

The Company will likely require additional capital in the future through equity or debt financings, partnerships, collaborations, or other sources to carry out the Company's planned development activities and to obtain regulatory approval for or to commercialize its product candidates. If additional capital is not secured when required, the Company may need to delay or curtail its operations until such funding is received. Various internal and external factors will affect whether and when the Company's product candidates become approved drugs. The regulatory approval and market acceptance of the Company's proposed future products (if any), length of time and cost of developing and commercializing these product candidates and/or failure of them at any stage of the drug approval process will materially affect the Company's financial condition and future operations. The Company believes its cash, cash equivalents, marketable securities and restricted cash at December 31, 2019 are sufficient to fund its current operations, however it will require additional capital to pursue preclinical and clinical activities, regulatory approval and the commercialization of its current and future product candidates.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of presentation and consolidation principles

The accompanying Consolidated Financial Statements include the accounts of Millendo Therapeutics, Inc. and its subsidiaries, and all intercompany amounts have been eliminated. The Consolidated Financial Statements have been prepared in conformity with U.S. generally accepted accounting principles ("GAAP"). Any reference in these notes to applicable guidance is meant to

refer to GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

The Consolidated Financial Statements include the accounts of the Company's subsidiaries in which the Company holds a controlling financial interest as of the financial statement date.

Use of estimates

The preparation of the Consolidated Financial Statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of expenses during the reporting period. Actual results could differ from those estimates. Due to the uncertainty of factors surrounding the estimates or judgments used in the preparation of the Consolidated Financial Statements, actual results may materially vary from these estimates. Estimates and assumptions are periodically reviewed and the effects of revisions are reflected in the financial statements in the period they are determined to be necessary.

Concentration of credit risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash, cash equivalents, marketable securities and restricted cash. The Company generally invests its cash in deposits with high credit quality financial institutions. Deposits at banks may exceed the insurance provided on such deposits. Additionally, the Company performs periodic evaluations of the relative credit standing of these financial institutions.

Cash and cash equivalents

The Company considers all highly liquid investments that have maturities of three months or less when acquired to be cash equivalents. Cash equivalents as of December 31, 2019 and 2018 consisted of money market funds.

Marketable securities

The Company classifies its marketable securities as available-for-sale securities and the securities are stated at fair value with realized gains and losses accounted for using the specific identification method. At December 31, 2018, the balance in the Company's accumulated other comprehensive income included activity related to the Company's available-for-sale marketable securities. There were no material realized gains or losses recognized on the maturity of available-for-sale securities during the years ended December 31, 2019 and 2018. As a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss for the same periods. There were no marketable securities held as of December 31, 2019.

Restricted cash

Restricted cash relates to amounts used to secure the Company's credit card facility balances held on deposit with major financial institutions, to collateralize a letter of credit in the name of the Company's landlord pursuant to a certain operating lease agreement, and to fund an escrow arrangement in connection with a sublease agreement also pursuant to that same operating lease agreement. The following table provides a reconciliation of the components of cash, cash equivalents, and restricted cash reported in the Company's consolidated balance sheets to the total of the amount presented in the Consolidated Statements of Cash Flows:

	December 31,	
	2019	2018
	(in thousands)	
Cash and cash equivalents	$ 62,478	$ 73,286
Restricted cash	1,034	45
Long-term restricted cash	—	439
Total cash, cash equivalents, and restricted cash shown in the Consolidated Statements of Cash Flows	$ 63,512	$ 73,770

Refundable tax credit

In connection with the acquisition of Alizé (see Note 1), the Company obtained French research tax credits (crédit d'impôt recherche) or ("CIR"). CIR earned are refundable or they can offset French corporate income tax due. Since the French research

tax credit can be recovered in cash, the Company has elected to treat this as a grant. During the year ended December 31, 2019 and 2018, the Company recognized a reduction of research and development expenses of $1.2 million and $1.4 million, respectively, and had a research tax credit receivable of $1.3 million and $2.3 million at December 31, 2019 and 2018, respectively.

Leases

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842),* which requires the Company as the lessee to recognize most leases on the balance sheet thereby resulting in the recognition of right-of-use assets and lease obligations for those leases currently classified as operating leases.

The Company adopted ASU 2016-02 using a modified retrospective transition approach as of January 1, 2019 and will not restate its comparative period financial information for effects of the standard or make the new required lease disclosures for periods before the date of adoption. The Company has elected to adopt the package of transition practical expedients and, therefore, have not reassessed (1) whether existing or expired contracts contain a lease, (2) lease classification for existing or expired leases or (3) the accounting for initial direct costs that were previously capitalized. As a result of the adoption of ASC 842, the Company recognized an operating lease liability of $2.0 million based on the present value of the minimum rental payments of the leases and a corresponding operating lease right-of-use ("ROU") asset of $0.9 million within the Company's Consolidated Balance Sheets. The Company's ROU asset is exclusive of any early lease termination obligations whereby future contractual lease payments exceed estimated sublease income.

Under ASC 842, the Company determines if an arrangement is a lease at contract inception. A lease exists when a contract conveys to the customer the right to control the use of identified property, plant, or equipment for a period of time in exchange for consideration. The definition of a lease embodies two conditions: (1) there is an identified asset in the contract that is land or a depreciable asset (i.e., property, plant, and equipment), and (2) the customer has the right to control the use of the identified asset.

The lease liabilities are initially and subsequently measured at the present value of the unpaid lease payments at the lease commencement date. When readily determinable, the Company uses the implicit rate in determining the present value of lease payments. When leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at the lease commencement date, including the lease term.

The ROU asset is initially measured at cost, which comprises the initial amount of the lease liability adjusted for lease payments made at or before the lease commencement date, plus any initial direct costs incurred less any lease incentives received. For operating leases, the ROU asset is subsequently measured throughout the lease term at the carrying amount of the lease liability, plus initial direct costs, plus (minus) any prepaid (accrued) lease payments, less the unamortized balance of lease incentives received. Lease expense for lease payments is recognized on a straight-line basis over the lease term. Refer to Note 9 for further details.

Fair value of financial instruments

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The asset's or liability's fair value measurement level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the Company's Consolidated Balance Sheets for cash equivalents, marketable securities, restricted cash, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to their short term nature. The carrying value of the Company's debt assumed from Alizé approximates fair value as of December 31, 2019 and 2018.

Redeemable noncontrolling interests

Redeemable noncontrolling interest represented the 16.4% interest in Alizé that was held by other investors until December 2018. The Company was subject to a put call agreement (see Note 1) with these investors, that was settled in December 2018, resulting in the Company acquiring the remaining issued and outstanding share capital of Alizé in exchange for cash and shares of the Company's common stock. The exchange ratio of shares was fixed at the amounts determined on the acquisition date. There were no redeemable noncontrolling interests outstanding as of December 31, 2019.

Other assets

Other assets includes property and equipment and other assets. Property and equipment, less accumulated depreciation, are recorded at cost and are depreciated on a straight-line basis over their estimated useful lives which range from three to five years except for leasehold improvements which are amortized over the shorter of the asset life or lease term. Repairs and maintenance costs are expensed as incurred. Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. The Company has not recognized any impairment of long-lived assets through December 31, 2019.

Deferred offering costs

The Company capitalizes costs that are directly associated with in-process equity financings until such financings are consummated, at which time such costs are recorded against the gross proceeds from the applicable financing. If a financing is abandoned, deferred offering costs are expensed. During the year ended December 31, 2018, the Company expensed $0.9 million in offering costs. The expense was recorded as a component of general and administrative expenses. No amounts were expensed during 2019.

Research and development expenses

Research and development costs are expensed as incurred and consist primarily of personnel expenses, costs of funding research performed by third parties, expenses incurred under agreements with contract manufacturing organizations, payments under third-party licensing agreements, consultant fees and expenses associated with outsourced professional scientific development services, expenses related to regulatory activities and allocated expense for facility costs. Milestone payment obligations incurred prior to regulatory approval of the product, which are accrued when the event requiring payment of the milestone occurs, are included in research and development expenses. Upfront milestone payments made to third parties who perform research and development services on the Company's behalf are expensed as services are rendered.

At the end of each reporting period, the Company compares payments made to third-party service providers to the estimated progress toward completion of the applicable research or development objectives. Such estimates are subject to change as additional information becomes available. Depending on the timing of payments to the service providers and the progress that the Company estimates has been made as a result of the service provided, the Company may record net prepaid or accrued expense relating to these costs. As of December 31, 2019 and 2018, the Company has not made any material adjustments to its prior estimates of accrued research and development expenses.

Stock-based compensation

The Company measures and recognizes compensation expense for all stock options awarded to employees and nonemployees based on the estimated fair market value of the award on the grant date. The Company uses the Black-Scholes option pricing model to value its stock option awards. The Company recognizes compensation expense on a straight-line basis over the requisite service period, which is generally the vesting period of the award. The Company accounts for forfeitures of stock options as they occur. Stock-based awards issued to nonemployees were revalued at each reporting period until the award vests.

October 1, 2018, the Company early adopted ASU 2018-7, *Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, which simplifies the accounting for share-based payments granted to nonemployees for goods and services. As a result of the adoption, stock-based awards issued to nonemployees are no longer

required to be revalued at each reporting period. The adoption of ASU No. 2018-7 did not have a material effect on the Consolidated Financial Statements.

Estimating the fair market value of options requires the input of subjective assumptions, including the estimated fair value of the Company's common stock, the expected life of the options, stock price volatility, the risk-free interest rate and expected dividends. The assumptions used in the Company's Black-Scholes option-pricing model represent management's best estimates and involve a number of variables, uncertainties and assumptions and the application of management's judgment, as they are inherently subjective.

Income taxes

The Company recognizes deferred tax assets and liabilities for temporary differences between the financial reporting basis and the tax basis of the Company's assets and liabilities and the expected benefits of net operating loss carryforwards. The impact of changes in tax rates and laws on deferred taxes, if any, applied during the period in which temporary differences are expected to be settled, is reflected in the Company's financial statements in the period of enactment. The measurement of deferred tax assets is reduced, if necessary, if, based on weight of the evidence, it is more likely than not that some, or all, of the deferred tax assets will not be realized. As of December 31, 2019 and 2018, the Company has concluded that a full valuation allowance is necessary for all of its net deferred tax assets. The Company had no material amounts recorded for uncertain tax positions, interest or penalties in the accompanying Consolidated Financial Statements.

In accordance with guidance issued by Financial Accounting Standards Board ("FASB"), companies should make and disclose a policy election as to whether they will recognize deferred taxes for basis differences expected to reverse as Global Intangible Low-Taxed Income ("GILTI") or whether they will account for GILTI as period costs if and when incurred. The Company has elected to recognize the resulting tax with respect to the GILTI provision as a period cost. No costs were incurred by the Company through December 31, 2019 as a result of GILTI.

Net loss per share

Basic loss per share of common stock is computed by dividing net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during each period. Diluted loss per share of common stock includes the effect, if any, from the potential exercise or conversion of securities, such as convertible debt, convertible preferred stock, preferred stock warrants, restricted stock, and stock options, which would result in the issuance of incremental shares of common stock. In computing the basic and diluted net loss per share, the weighted-average number of shares of common stock remains the same for both calculations due to the fact that when a net loss exists, dilutive shares are not included in the calculation as the impact is anti-dilutive.

The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares of common stock outstanding, as they would be anti-dilutive (amounts shown as common stock equivalents):

	Year ended December 31,	
	2019	**2018**
Stock options	2,498,606	1,764,287
Common stock warrants	17,125	17,125
BSA and BSPCE warrants	95,567	156,719
	2,611,298	1,938,131

Segment information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one segment.

Foreign currency

Results of foreign operations are translated from their functional currency into U.S. dollars (reporting currency) using average exchange rates in effect during the year, while assets and liabilities are translated into U.S. dollars using exchange rates in effect at the balance sheet date. The resulting translation adjustments are recorded in accumulated other comprehensive loss. Transaction gains and losses resulting from exchange rate changes on transactions denominated in currencies other than the

functional currency are included in income in the period in which the change occurs and reported within other expenses in the consolidated statements of operations and comprehensive loss.

Recent accounting pronouncements

In January 2020, the FASB issued ASU 2020-01, *Investments-Equity Securities (Topic 321), Investments-Equity Method and Joint Ventures (Topic 323), and Derivatives and Hedging (Topic 815).* ASU 2020-01 states any equity security transitioning from the alternative method of accounting under Topic 321 to the equity method, or vice versa, due to an observable transaction will be remeasured immediately before the transition. In addition, the ASU clarifies the accounting for certain non-derivative forward contracts or purchased call options to acquire equity securities stating such instruments will be measured using the fair value principles of Topic 321 before settlement or exercise. The ASU is effective for fiscal years beginning after December 15, 2020, and will be applied on a prospective basis. Early adoption is permitted. The Company is in the process of evaluating the impact of this new guidance on its consolidated financial statements and related disclosures.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740) - Simplifying the Accounting for Income Taxes.* ASU 2019-12 simplifies the accounting for income taxes by removing exceptions within the general principles of Topic 740 regarding the calculation of deferred tax liabilities, the incremental approach for intraperiod tax allocation, and calculating income taxes in an interim period. In addition, the ASU adds clarifications to the accounting for franchise tax (or similar tax), which is partially based on income, evaluating tax basis of goodwill recognized from a business combination, and reflecting the effect of any enacted changes in tax laws or rates in the annual effective tax rate computation in the interim period that includes the enactment date. The ASU is effective for fiscal years beginning after December 15, 2020, and will be applied either retrospectively or prospectively based upon the applicable amendments. Early adoption is permitted. The Company is in the process of evaluating the impact of this new guidance on its consolidated financial statements and related disclosures.

In July 2019, the FASB issued ASU 2019-07, *Codification Updates to SEC Sections - Amendments to SEC Paragraphs Pursuant to SEC Final Rule Releases No. 33-10532, Disclosure Update and Simplification, and Nos. 33-10231 and 33-10442, Investment Company Reporting Modernization and Miscellaneous Updates*. ASU 2019-07 clarifies or improves the disclosure and presentation requirements of a variety of codification topics by aligning them with the SEC's regulations, thereby eliminating redundancies and making the codification easier to apply. ASU 2019-07 became effective upon issuance and the adoption of ASU 2019-07, which is applied prospectively, did not have an impact on the Company's consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820) Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement*. ASU 2018-13 resulted in certain modifications to fair value measurement disclosures, primarily related to level 3 fair value measurements. The new standard is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019, and early adoption is permitted. The Company is currently evaluating the potential impact of the adoption of this standard on its disclosures.

In June 2018, the FASB issued ASU 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*. ASU 2018-07 is intended to reduce the cost and complexity and to improve financial reporting for non-employee share-based payments. The ASU expands the scope of Topic 718, Compensation-Stock Compensation (which currently only includes share-based payments to employees), to include share-based payments issued to non-employees for goods or services. Consequently, the accounting for share-based payments to non-employees and employees will be substantially aligned. This update is effective for annual and interim periods beginning after December 15, 2018 with early adoption permitted. Upon transition, entities will remeasure unsettled liability-classified awards and any unmeasured equity-classified awards for non-employees at fair value as of the adoption date. A cumulative-effect adjustment to retained earnings will be required as of the beginning of the fiscal year of adoption. The Company adopted ASU No. 2018-07 on October 1, 2018, which did not have a material effect on the consolidated financial statements.

In March 2018, the FASB issued ASU 2018-05, *Income Taxes (Topic 740): Amendments to SEC Paragraphs Pursuant to SEC Staff Accounting Bulletin No. 118*, which amends *Income Taxes (Topic 740) b*y incorporating the Securities and Exchange Commission's ("SEC") Staff Accounting Bulletin 118 ("SAB 118") issued on December 22, 2017. SAB 118 provide guidance on accounting for the effects of the Tax Act. The Company recognized the income tax effects of the Tax Act in the 2018 Consolidated Financial Statements in accordance with SAB 118. See Note 12 of the consolidated financial statements for additional disclosures.

In August 2016, the FASB issued ASU 2016-15, *Statement of Cash Flows (Topic 230) Classification of Certain Cash Receipts and Cash Payments,* which will make eight targeted changes to how cash receipts and cash payments are presented and classified in the statement of cash flows. This standard was effective January 1, 2019 and required adoption on a retrospective

basis unless it is impracticable to apply, in which case the Company would be required to apply the amendments prospectively as of the earliest date practicable. The Company adopted this standard which did not have a material impact on its consolidated financial statements and related disclosures.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326) Measurement of Credit Losses on Financial Instruments*, which replaces the incurred loss impairment methodology in current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. Additionally, ASU 2016-13 requires a financial asset measured at amortized cost basis to be presented at the net amount expected to be collected through the use of an allowance of expected credit losses. In May 2019, the FASB issued ASU 2019-05, *Financial Instruments - Credit Losses (Topic 326) Targeted Transition Relief*, which amends ASU 2016-13 by providing entities with an option to irrevocably elect the fair value option to be applied on an instrument-by-instrument basis for eligible financial instruments that are within the scope of Topic 326. The fair value option election does not apply to held-to-maturity debt securities. In November 2019, the FASB issued ASU 2019-10, *Financial Instruments - Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842)*, which finalized effective date delays for private companies, not-for-profit organizations, and certain smaller reporting companies applying the credit losses, leases, and hedging standards. Also in November 2019, the FASB issued ASU 2019-11, *Codification Improvements to Topic 326, Financial Instruments - Credit Losses*, which provides clarity about certain aspects of the amendments in ASU 2016-13. ASU 2016-13, as amended, is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years, and requires a modified retrospective approach. The Company is in the process of evaluating the impact of this new guidance on its consolidated financial statements and related disclosures.

In January 2016, the FASB issued authoritative guidance under ASU 2016-1, *Financial Instruments—Overall (Subtopic 825-10): Recognition and Measurement of Financial Assets and Financial Liabilities*. ASU 2016-1 revises the classification, measurement and disclosure of investments in equity securities. The Company adopted this standard effective January 1, 2018. The adoption of ASU 2016-1 did not have an impact on the Company's consolidated financial statements.

Subsequent events

Subsequent events were evaluated through the filing date of this Annual Report.

3. OvaScience Merger

As described in Note 1, Private Millendo merged with the Company in December 2018. The Merger was accounted for as a reverse recapitalization with Private Millendo as the accounting acquirer. The primary pre-combination assets of OvaScience was cash, cash equivalents and marketable securities. Under reverse recapitalization accounting, the assets and liabilities of OvaScience were recorded at their fair value which approximated book value due to the short-term nature of the instruments. No goodwill or intangible assets were recognized. Consequently, the Consolidated Financial Statements of Millendo reflect the operations of OvaScience for accounting purposes together with a deemed issuance of shares, equivalent to the shares held by the former stockholders of the legal acquirer and a recapitalization of the equity of the accounting acquirer.

As part of the reverse recapitalization, the Company obtained approximately $40.2 million of cash and marketable securities. The Company also obtained prepaids and other assets of $1.3 million and assumed payables and accruals of approximately $3.5 million, which includes a $1.4 million lease termination liability. All of the development programs have been terminated and were deemed to have no value at the transaction date and the Company is winding down the legacy OvaScience operations.

Additionally, the Company incurred approximately $1.8 million in severance costs as a result of resignations of executive officers immediately prior to the Merger and approximately $43,000 in share based compensation expense as a result of the acceleration of vesting of stock options at the time of Merger.

4. Marketable Securities

The following summarizes the available-for-sale securities held as of December 31, 2018 (amounts in thousands):

	December 31, 2018			
	Amortized cost	Unrealized gains	Unrealized losses	Fair value
U.S. government agency	$ 2,994	$ —	$ —	$ 2,994
Corporate debt securities	$ 1,391	$ —	$ —	$ 1,391

Marketable securities were acquired in connection with the Merger. There were immaterial unrealized losses recorded from the date of Merger through December 31, 2018. The Company does not have any marketable securities as of December 31, 2019. Available-for-sale securities held at December 31, 2018 had maturities of less than one year.

5. Fair Value Measurements

The following table presents the Company's assets and liabilities that are measured at fair value on a recurring basis (amounts in thousands):

	December 31, 2019		
	(Level 1)	(Level 2)	(Level 3)
Assets			
Money market funds (included in cash and cash equivalents)	$ 59,382	$ —	$ —
Marketable securities - U.S. government agency	$ —	$ —	$ —
Marketable securities - Corporate debt securities	$ —	$ —	$ —

	December 31, 2018		
	(Level 1)	(Level 2)	(Level 3)
Assets			
Money market funds (included in cash and cash equivalents)	$ 25,145	$ —	$ —
Marketable securities - U.S. government agency	$ —	$ 2,994	$ —
Marketable securities - Corporate debt securities	$ —	$ 1,391	$ —

The fair value of the Company's marketable securities is estimated using observable market-based inputs such as quoted prices, interest rates and yield curves or Level 2 inputs.

The Company's preferred stock warrants were classified as liabilities, recorded at fair value and subject to re-measurement at each balance sheet date until they were converted into common stock warrants in connection with the completion of the Merger. The common stock warrants are equity classified as of the Merger date and are no longer subject to remeasurement.

The reconciliation of the preferred stock warrant liability measured at fair value, until the reclassification into equity at the time of the Merger, on a recurring basis using significant unobservable inputs (Level 3) was as follows (amounts in thousands):

	Preferred stock warrant liability
Balance at January 1, 2018	$ 139
Additions	(40)
Change in fair value	(99)
Balance at December 31, 2018	$ —

The Series A and Series B preferred stock warrant liabilities were estimated using an option pricing model. The significant assumptions used in valuing the warrants include expected term, expected volatility, risk-free interest rate and expected dividend yield. As of Merger date, immediately prior to reclassifying the warrants to equity, the significant weighted-average assumptions were as follows:

	Year ended December 31,
	2018
Expected term (in years)	1.75
Expected volatility	71 %
Risk free rate	2.58 %
Dividend yield	— %

6. Accrued Expenses

Accrued expenses consist of (amounts in thousands):

	December 31,	
	2019	2018
Compensation and related benefits	$ 2,042	$ 3,537
Professional fees	2,929	1,140
Preclinical and clinical costs	1,820	1,811
Lease termination	—	630
Insurance premiums	1,423	—
Other	852	512
Total	$ 9,066	$ 7,630

In connection with the adoption of ASC 842, the new leasing standard, on January 1, 2019, the lease termination balance as of December 31, 2018 was reclassified into the Company's operating lease liability.

7. Debt

Bpifrance Reimbursable Advance

In December 2017, in connection with its acquisition of Alizé (see Note 1), the Company assumed €0.7 million of debt that Alizé had outstanding with Bpifrance Financing ("Bpifrance"). The original advance amount of €0.8 million ("the Bpifrance Advance") was provided to Alizé as an innovation aid that required Alizé to carry out certain activities related to its livoletide clinical development program and incur a certain level of program expenditures. No interest is charged or accrued under the advance.

The Company is required to make quarterly principal payments, which began in December 2016 and continue through September 2021. The quarterly principal payments escalate over the repayment period beginning with €17,500 per quarter and increasing to €50,000 through maturity. In addition to the quarterly payments, the Company could be obligated to pay on an accelerated basis the principal payments, if applicable, no later than March 31st of each year starting from January 1, 2016, a reimbursement annuity equal to 20% of the proceeds generated by the Company from license, assignment or use of the livoletide. Under no circumstance would the Company be required to reimburse to Bpifrance principal amounts greater than the original advance it received.

The Company is permitted to repay the Bpifrance Advance at any time, at which point it would be released from all commitments and obligations under the Bpifrance Advance agreement. The Bpifrance Advance Agreement does not contain any ongoing financial covenants.

At December 31, 2019, the balance outstanding was $0.4 million (€0.3 million).

Convertible promissory notes

In August 2018, the Company issued convertible promissory notes (as amended) to several of its existing investors and received cash proceeds of $8.0 million. The notes accrued simple interest of 6.0% per annum and all principal and interest was due at maturity, if not converted. Upon consummation of the Merger, the outstanding principal and interest converted into 499,504 shares of the Company's common stock. The Company recorded debt issuance costs of $0.5 million in connection with the promissory notes. The debt discount was amortized into interest expense over the term of the promissory notes using the effective interest method. At the time of conversion, the unamortized debt discount of $0.4 million was reclassified to equity. For the year ended December 31, 2018, the Company recognized interest expense of $0.2 million of which $52,000 was attributable to the amortization of the debt discount.

8. License Agreements

University of Michigan License Agreement

In June 2013, the Company entered into a license agreement with the Regents of the University of Michigan (the "University of Michigan") for a worldwide, exclusive, sublicensable license to the University of Michigan's interest in certain patent rights jointly owned with the Company, covering the use of ATR-101 for the treatment of certain indications (the "UM License Agreement"). The Company is obligated to make payments to the University of Michigan totaling up to $2.5 million upon the achievement of certain development and commercial milestones. No amounts were paid in 2018 or 2019 related to the achievement of development or commercial milestones. During the year ended December 31, 2019, $0.1 million was paid in order to extend the milestone achievement date of certain development milestones. The Company is also required to pay the University of Michigan a low-single digit royalty percentage on net sales of applicable products, if any.

In addition, $20,000 in annual minimum royalties are due under the UM License Agreement for each of 2020 through 2023. Further, beginning in 2024, the Company is required to pay an annual fee of $0.2 million which is creditable against royalties due, if any, until the expiration or termination of the UM License Agreement.

Assignment agreement with Erasmus University Medical Center and the University of Turin

In connection with its acquisition of Alizé, the Company assumed Alizé's obligations under an assignment agreement with Erasmus University Medical Center, the University of Turin and certain individuals (collectively "the Assignors"), for certain patents and patent applications relating to livoletide.

In connection with the assignment, the Company agreed to pay the Assignors a flat, low single digit royalty on net commercial sales of products containing livoletide that are covered by the claims of the assigned intellectual property. Further, upon approval of livoletide by the FDA or EMA, the Company is required to pay the Assignors CDN $100,000, which amount will be deducted from any future royalty payments due to the Assignors. The Company also agreed to pay the Assignors a low single digit percentage of any amounts received in connection with its license of the assigned intellectual property or products containing livoletide that are covered by the claims of the assigned intellectual property.

License Agreement with Roche

On October 16, 2018, the Company entered into a license agreement with F. Hoffmann-La Roche Ltd and Hoffman-La Roche Inc. (collectively, "Roche"), for a worldwide, exclusive license to Roche's interest in certain patent rights and know-how covering, among other things, the use of a neurokinin 3 receptor antagonist (the "Roche License Agreement").

As consideration for the rights granted to the Company under the Roche License Agreement, the Company agreed to pay Roche an up-front payment. Under the terms of the Roche License Agreement, the Company is also obligated to make significant milestone and royalty payments in connection with the attainment of certain development steps and the sale of resulting products with respect to the neurokinin 3 receptor antagonist. In addition, the Company is required to share a portion of any net proceeds received in connection with certain agreements that it may enter into with third parties to develop and commercialize the neurokinin 3 receptor antagonist.

9. Commitments and Contingencies

Operating leases

The Company has noncancelable operating leases for office and laboratory space which have remaining lease terms between one and six years. In connection with the Merger, the Company assumed a sublease agreement for office and laboratory space located in Waltham, Massachusetts. The sublease commenced on January 15, 2019 and expires on November 30, 2020. The total minimum sublease rentals to be received under the Waltham, Massachusetts agreement is $0.6 million. The remaining sublease rentals to be received as of December 31, 2019 is $0.3 million. In February 2019 and October 2018, the Company entered into two additional noncancelable operating leases for office space in Ann Arbor, Michigan for the Company's headquarters; one that the Company took possession of in April 2019, and the other that the Company took possession of in July 2019. One of its leases in Ann Arbor, Michigan expires in June 2024 and the other expires in March 2024. In April 2019,

the Company entered into a lease agreement for office space in Lexington, Massachusetts to expand its operations. Lease agreements generally do not require material variable lease payments, residual value guarantees or restrictive covenants.

As of December 31, 2019, the operating lease ROU asset and the operating lease liabilities were $3.3 million and $4.1 million, respectively. The weighted average discount rate used to account for the Company's operating leases under ASC 842 is the Company's estimated incremental borrowing rate of 7.0%. The Company has options to extend certain of its leases for another five to nine years. These options to extend were not recognized as part of the Company's measurement of the ROU assets and operating lease liabilities for the year ended December 31, 2019. The weighted average remaining term of the Company's noncancelable operating leases is 3.71 years.

Rent expense related to the Company's operating leases was approximately $0.7 million and $0.2 million for the years ended December 31, 2019 and 2018, respectively. The Company recognizes rent expense on a straight-line basis over the lease period and has accrued for rent expense incurred but not yet paid. Cash paid for amounts included in the measurement of the lease liabilities was approximately $1.5 million during the year ended December 31, 2019. The Company received approximately $0.3 million in sublease payments related to its Waltham, Massachusetts lease during the year ended December 31, 2019. Future minimum rental payments under the Company's noncancelable operating leases at December 31, 2019 is as follows (amounts in thousands):

Year Ending December 31,		
2020	$	1,803
2021		805
2022		828
2023		851
2024		347
Thereafter		45
Total	$	4,679
Present Value Adjustment		(533)
Lease liability at December 31, 2019	$	4,146

Employment benefit plan

The Company maintains a defined contribution 401(k) plan in which employees may contribute up to 100% of their salary and bonus, subject to statutory maximum contribution amounts. The Company contributes a safe harbor minimum contribution equivalent to 3% of employees' compensation. The Company generally assumes all administrative costs of the plan. For the years ended December 31, 2019 and 2018, the expense relating to the contributions made was $0.2 million and $0.1 million, respectively.

Litigation

Liabilities for loss contingencies arising from claims, assessments, litigation, fines, penalties, and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated.

On November 9, 2016, a purported shareholder derivative action was filed in the Business Litigation Session of the Suffolk County Superior Court in the Commonwealth of Massachusetts (*Cima v. Dipp*, No. 16-3443-BLS1 (Mass. Sup. Ct.)) against certain former officers and directors of OvaScience and one current director of the Company (a former director of OvaScience) and OvaScience as a nominal defendant alleging breaches of fiduciary duty, unjust enrichment, abuse of control, gross mismanagement and corporate waste for purported actions related to OvaScience's January 2015 follow-on public offering. On February 22, 2017, the court approved the parties' joint stipulation to stay all proceedings in the action until further notice. Following a status conference in December 2017, the stay was lifted. On January 25, 2018, at the parties' request, the court entered a second order staying all proceedings in the action until further order of the court. On March 2, 2020, the parties submitted a status report requesting that the Court continue the stay. The Company believes that the complaint is without merit and intends to defend against the litigation. There can be no assurance, however, that the Company will be successful. At present, the Company is unable to estimate potential losses, if any, related to the lawsuit.

On March 24, 2017, a purported shareholder class action lawsuit was filed in the U.S. District Court for the District of Massachusetts (*Dahhan v. OvaScience, Inc.*, No. 1:17-cv-10511-IT (D. Mass.)) against OvaScience and certain former officers

and directors of OvaScience alleging violations of Sections 10(b) and 20(a) of the Exchange Act (the "Dahhan Action"). On July 5, 2017, the court entered an order approving the appointment of Freedman Family Investments LLC as lead plaintiff, the firm of Robins Geller Rudman & Dowd LLP as lead counsel and the Law Office of Alan L. Kovacs as local counsel. Plaintiff filed an amended complaint on August 25, 2017. The Company filed a motion to dismiss the amended complaint, which the court denied on July 31, 2018. On August 14, 2018, the Company answered the amended complaint. On December 9, 2019, the Court granted leave for plaintiff to file a second amended complaint under seal and permitted defendants to file a motion to strike the second amended complaint. On December 30, 2019, the Court granted the parties' joint motion to stay all proceedings in the case pending mediation. On March 3, 2020, the parties conducted a mediation session. As the mediation was unsuccessful, the parties are resuming discovery. The Company believes that the amended complaint and the second amended complaint are without merit and intends to defend against the litigation. There can be no assurance, however, that the Company will be successful. A resolution of this lawsuit adverse to the Company or the other defendants could have a material effect on the Company's consolidated financial position and results of operations. At present, the Company is unable to estimate potential losses, if any, related to the lawsuit.

On July 27, 2017, a purported shareholder derivative complaint was filed in the U.S. District Court for the District of Massachusetts (*Chiu v. Dipp*, No. 1:17-cv-11382-IT (D. Mass.)) against OvaScience, as a nominal defendant, certain former officers and directors of OvaScience and one current director of the Company (a former director of OvaScience) alleging breach of fiduciary duty, unjust enrichment and violations of Section 14(a) of the Exchange Act alleging that compensation awarded to the director defendants was excessive and seeking redress for purported actions related to OvaScience's January 2015 follow-on public offering and other public statements. On September 26, 2017, the plaintiff filed an amended complaint which eliminated all claims regarding allegedly excessive director pay and additionally alleged claims of abuse of control and corporate waste. On October 27, 2017, the defendants filed a motion to dismiss the amended complaint. The court heard oral argument on the motion to dismiss on April 5, 2018. On April 13, 2018, the court granted the defendants' motion to dismiss the amended complaint for failure to state a claim for relief under Section 14(a). The court also dismissed the plaintiffs' pendent state law claims without prejudice, based on lack of subject matter jurisdiction. On April 25, 2018, the plaintiffs moved for leave to amend the complaint, and to stay this case pending the outcome of the Dahhan Action. The Company does not believe that the proposed amended complaint cures the defects in the current complaint, but informed plaintiffs' counsel that, in the interest of judicial economy, defendants would not oppose the proposed amendment if the court would consider staying the case pending the resolution of the Dahhan Action. On April 27, 2018, the court granted the plaintiffs' motion for leave to amend the complaint and for a stay. On April 30, 2018, the plaintiffs filed their second amended complaint. On May 23, 2018, the court entered an order staying this case pending the resolution of the Dahhan Action. The Company believes that the complaint is without merit and intends to defend against the litigation. There can be no assurance, however, that the Company will be successful. At present, the Company is unable to estimate potential losses, if any, related to the lawsuit.

In addition to the matters described above, the Company may be a party to litigation and subject to claims incident to the ordinary course of business from time to time. Regardless of the outcome, litigation can have an adverse impact on the Company because of defense and settlement costs, and diversion of management resources.

10. Common Stock and Convertible Preferred Stock

Common stock

In December 2019, the Company sold a total of 4,791,667 shares of its common stock pursuant to the Underwriting Agreement with the Underwriters, for total net proceeds of approximately $26.5 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company. The price to the public in this offering was $6.00 per share and resulted in the sale of 4,166,667 shares of the Company's common stock for net proceeds of approximately $23.0 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company. In addition, the Underwriters purchased an additional 625,000 shares of the Company's common stock at the public offering price of $6.00 per share pursuant to a purchase option granted to them under the Underwriting Agreement, resulting in net proceeds of approximately $3.5 million, after deducting underwriting discounts and commissions.

Upon completion of the Merger in December 2018, the Company issued shares of its common stock to Private Millendo's stockholders, at an exchange ratio of 0.0744 shares of the Company's common stock, for each share of Private Millendo common stock outstanding immediately prior to the Merger. In addition, the Company sold 1,230,158 shares of common stock at $16.26 per share and received $18.7 million in net proceeds. Concurrent with the Merger, the Company issued 499,504 shares upon conversion of the promissory notes (see Note 7).

In connection with the acquisition of the remaining 16.4% of Alizé, the Company issued 450,371 shares of its common-1 stock. Upon consummation of the Merger, the common-1 shares were converted into common stock on a 1:1 basis.

During the year ended December 31, 2019, stock options were exercised for 97,225 shares of common stock. During the year ended December 31, 2018, the Company issued no shares of common stock in connection with the exercise of stock options.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Subject to preferences that may apply to any outstanding preferred stock, holders of common stock are entitled to receive ratably any dividends that the Company's board of directors may declare out of funds legally available for that purpose on a non-cumulative basis. No dividends had been declared through December 31, 2019.

Convertible preferred stock

In connection with the Alizé acquisition, the Company issued 6,540,763 and 20,636,179 shares of its Series A-1 and Series B-1 preferred stock, respectively. No shares were issued and outstanding as of December 31, 2019.

The Company had Series A, Series A-1, Series B and Series B-1 convertible preferred stock, that were classified outside of stockholders' equity (deficit) because the shares contain deemed liquidation rights that were contingent redemption features not solely within the control of the Company. As a result, all of the Company's convertible preferred stock was classified as temporary equity.

Upon completion of the Merger in December 2018, all of the outstanding shares of the Company's convertible preferred stock were converted into an aggregate of 6,759,109 shares of common stock. As of December 31, 2019, no preferred stock was issued or outstanding.

Dividends

The holders of Series B and Series B-1 preferred stock, in preference to holders of any other class or series of the Company's stock, were entitled to non-cumulative dividends at a rate of 8.0%, if and when declared by the Company's board of directors. After payment to the holders of the Series B and Series B-1 preferred stock, the holders of Series A and Series A-1 preferred stock, in preference to holders of any other class or series of the Company's stock, were entitled to non-cumulative dividends at a rate of 8.0%, if and when declared by the Company's board of directors. In the event a dividend was declared to common stockholders, holders of Series A, Series A-1, Series B and Series B-1 preferred stock would also receive an equivalent dividend on an "as-converted" basis. No dividends were declared or paid during the years ended December 31, 2019 and 2018.

Voting

The holders of Series A, Series A-1, Series B and Series B-1 preferred stock were entitled to one vote for each share of common stock into which their shares of preferred stock may have converted and, subject to certain preferred stock class votes specified in the Company's certificate of incorporation or as required by law, the holders of the preferred stock and common stock voted together on an as-converted basis.

Liquidation preference

In the event of a liquidation, dissolution or winding up of the Company, either voluntary or involuntary, or in the event of a deemed liquidation event, which includes a sale of the Company as defined in the Company's articles of incorporation, holders of Series A, Series A-1, Series B, and B-1 preferred stock are entitled to receive, in preference to all other stockholders, an amount equal to their original investment amount plus any declared and unpaid dividends. If upon the occurrence of such event, the assets and funds available for distribution are insufficient to pay such holders the full amount to which they are entitled, then the entire assets and funds legally available for distribution shall be distributed ratably among the holders of the Series B and Series B-1 preferred stock in proportion to the full amounts to which they would otherwise be entitled.

After payment in full of the liquidation preference of the Series B and Series B-1 preferred stock, holders of Series A and Series A-1 preferred stock are entitled to receive, in preference to all holders of common stock, an amount equal to their original investment amount plus any declared and unpaid dividends. If upon the occurrence of such event, the assets and funds available for distribution are insufficient to pay such holders the full amount to which they are entitled, then the entire remaining assets and funds legally available for distribution shall be distributed ratably among the holders of the Series A and Series A-1 preferred stock in proportion to the full amounts to which they would otherwise be entitled.

After payment of the liquidation preference on shares of Series A, Series A-1, Series B, and Series B-1 preferred stock has been made, any remaining assets shall be distributed ratably to common and preferred stockholders, on an as converted basis, until such time as each holder of preferred stock has received an aggregate amount per share equal to three times the original issue price of such share. Thereafter, the remaining assets of the company available for distribution shall be distributed ratably to holders of common stock.

Conversion

Each share of Series A, Series A-1, Series B, and Series B-1 preferred stock was convertible into common stock at any time at the option of the holder thereof at the conversion price then in effect. All shares of Series A, Series A-1, Series B and Series B-1 preferred stock were convertible into common stock at the affirmative election of the holders of at least a majority of the outstanding shares of preferred stock at the conversion price then in effect. The conversion price for the Series A and Series A-1 preferred stock was $1.00 and the conversion price for the Series B and Series B-1 preferred stock was $1.49776 (each subject to adjustments upon the occurrence of certain dilutive events). Upon any automatic conversion, any declared and unpaid dividends would be payable to the holders of preferred stock.

Convertible preferred stock warrants

Prior to completing the Merger in December 2018, the Company had issued warrants to purchase up to 110,000 shares of Series A preferred stock (Series A warrants) and up to 120,179 shares of Series B preferred stock (Series B warrants). The Series A warrants and Series B warrants expire in April 2024 and July 2026, respectively.

The warrants were liability classified because they were exercisable for contingently redeemable preferred stock, and the value of the warrants were remeasured at each reporting period (see Note 5). Upon completion of the Merger, the warrants automatically converted into warrants for common stock. As of December 31, 2019, there were 17,125 common stock warrants outstanding with a weighted average exercise price of $16.93 per share.

11. Stock-Based Compensation

On June 11, 2019, the Company held its 2019 Annual Meeting of Stockholders (the “Annual Meeting”). At the Annual Meeting, the Company’s stockholders approved the Company’s 2019 Equity Incentive Plan (the “2019 Plan”) and the Company’s 2019 Employee Stock Purchase Plan (the “2019 ESPP,” and together with the 2019 Plan, the “Plans”). The 2019 Plan is the successor to the Private Millendo 2012 Stock Plan and the OvaScience 2012 Stock Incentive Plan (each, as amended, the “Prior Plans”) and allows the Company to grant stock options, restricted stock unit awards and other awards at levels determined appropriate by the Company’s Board of Directors (the “Board”) or the Compensation Committee of the Board. No additional awards will be granted under either of the Prior Plans. The 2019 ESPP enables employees to purchase shares of the Company’s common stock through offerings of rights to purchase the Company’s common stock to all eligible employees. The Plans were adopted by the Board on April 29, 2019, subject to approval by the Company’s stockholders, and became effective with such stockholder approval on June 11, 2019. Outstanding awards under the Prior Plans continue to be subject to the terms and conditions of the Prior Plans.

The aggregate number of shares of the Company's common stock initially reserved for issuance under the 2019 Plan was 2,919,872 shares, which is the sum of (i) 534,320 new shares, (ii) the number of unallocated shares remaining available for grant under the Prior Plans as of the effective date of the 2019 Plan, and (iii) the Prior Plans' Returning Shares (as defined below), as such shares become available from time to time. The number of shares of the Company's common stock reserved for issuance under the 2019 Plan will automatically increase on January 1 of each year, for a period of ten years, from January 1, 2020 continuing through January 1, 2029, by 4% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by the Board.

The term "Prior Plans' Returning Shares" refers to the following shares of the Company's common stock subject to any outstanding stock award granted under either of the Prior Plans: shares of common stock subject to awards that (i) expire or terminate for any reason prior to exercise or settlement; (ii) are forfeited because of the failure to meet a contingency or condition required to vest such shares or otherwise return to the Company; or (iii) are reacquired, withheld (or not issued) to satisfy a tax withholding obligation in connection with an award or to satisfy the purchase price or exercise price of a stock award. The foregoing includes shares subject to outstanding awards under the OvaScience 2011 Stock Incentive Plan that expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right.

The following shares of the Company's common stock (collectively, the "2019 Plan Returning Shares") will also become available again for issuance under the 2019 Plan: (i) any shares subject to a stock award that are not issued because such stock award expires or otherwise terminates without all of the shares covered by such stock award having been issued; (ii) any shares subject to a stock award that are not issued because such stock award is settled in cash; (iii) any shares issued pursuant to a stock award that are forfeited back to or repurchased by the Company because of the failure to meet a contingency or condition required for the vesting of such shares; and (iv) any shares reacquired by the Company in satisfaction of tax withholding obligations on a stock award or as consideration for the exercise or purchase price of a stock award.

The aggregate number of shares of the Company's common stock that may be issued under the 2019 ESPP is 133,580 shares, plus the number of shares of the Company's common stock that are automatically added on January 1st of each year, for a period of up to ten years, from January 1, 2020 continuing through January 1, 2029, by 1% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by the Board.

The Company measures employee and nonemployee stock-based awards at grant-date fair value and records compensation expense on a straight-line basis over the vesting period of the award. Stock-based awards issued to nonemployees are revalued until the award vests.

The Company recorded stock-based compensation expense in the following expense categories of its accompanying consolidated statements of operations and comprehensive loss for the years ended December 31, 2019 and 2018 (amounts in thousands):

	Year Ended December 31,	
	2019	2018
Research and development	$ 1,299	$ 606
General and administrative	3,018	821
Total	$ 4,317	$ 1,427

Options issued may have a contractual life of up to 10 years and may be exercisable in cash or as otherwise determined by the board of directors. Vesting generally occurs over a period of not greater than four years.

The following table summarizes the activity related to stock option grants to employees and nonemployees for the years ended December 31, 2019 and 2018:

	Shares	Weighted-average exercise price share	Weighted-average remaining contractual life (years)
Outstanding at January 1, 2018	703,479	$ 4.91	7.8
Options assumed from OvaScience Merger	423,316	78.70	
Granted	776,140	15.82	
Cancelled	(72,049)	16.40	
Forfeited	(66,599)	8.54	
Outstanding at December 31, 2018	1,764,287	26.81	8.0
Granted	1,225,901	9.73	
Exercised	(97,225)	3.71	
Forfeited	(394,357)	40.42	
Outstanding at December 31, 2019	2,498,606	$ 17.18	7.7
Vested and exercisable at December 31, 2019	984,264	$ 26.42	5.6
Vested and expected to vest at December 31, 2019	2,498,606	$ 17.18	7.7

As of December 31, 2019, the unrecognized compensation cost related to 1,514,342 unvested stock options expected to vest was $9.2 million. This unrecognized compensation will be recognized over an estimated weighted-average amortization period of 2.8 years. The aggregate intrinsic value of options exercised during the year ended December 31, 2019 was $0.7 million. There were no options exercised during the year ended December 31, 2018. The aggregate intrinsic value of options outstanding and options exercisable as of December 31, 2019 was $1.2 million and $1.2 million, respectively. The options

granted during the years ended December 31, 2019 and 2018, had an estimated weighted average grant date fair value of $6.74 and $9.72, respectively.

The fair value of options is estimated using the Black-Scholes option pricing model, which takes into account inputs such as the exercise price, the value of the underlying common stock at the grant date, expected term, expected volatility, risk-free interest rate and dividend yield. The fair value of each grant of options during the years ended December 31, 2019 and 2018 was determined using the methods and assumptions discussed below.

- The expected term of employee options with service-based vesting is determined using the "simplified" method, as prescribed in SEC's Staff Accounting Bulletin ("SAB") No. 107, whereby the expected life equals the arithmetic average of the vesting term and the original contractual term of the option due to the Company's lack of sufficient historical data. The expected term of nonemployee options is equal to the contractual term.
- The expected volatility is based on historical volatilities of similar entities within the Company's industry which were commensurate with the expected term assumption as described in SAB No. 107.
- The risk-free interest rate is based on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected term.
- The expected dividend yield is 0% because the Company has not historically paid, and does not expect for the foreseeable future to pay, a dividend on its common stock.
- Prior to the Merger, the Company's common stock was not publicly traded. The Company's board of directors periodically estimated the fair value of the Company's common stock considering, among other things, contemporaneous valuations of its common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants 2013 Practice Aid, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation.* Following the Merger, the fair market value of the Company's common stock is determined based on the closing price of its common stock on the Nasdaq Capital Market.

The grant date fair value of each option grant was estimated throughout the year using the Black-Scholes option-pricing model using the following assumptions for the Plan:

	Year Ended, December 31, 2019	Year Ended, December 31, 2018
Expected term (in years)	6.02	6.08
Expected volatility	80 %	66 %
Risk-free interest rate	2.22 %	2.77 %
Expected dividend yield	0 %	0 %
Fair market value of common stock	$ 9.73	$ 15.82

At the time of the Alizé acquisition, Alizé had 6,219 non-employee (BSA) warrants and 5,360 employee (BSPCE) warrants outstanding, which have weighted-average exercise prices of €80.06 and €83.40, respectively. As of December 31, 2019, all BSAs and BSPCEs were vested. During the year ended December 31, 2019, 1,310 BSPCE warrants were exercised resulting in the issuance of 17,713 shares of the Company's common stock. In addition, during the year ended December 31, 2019, a total of 3,210 BSA and BSPCE warrants were forfeited. As of December 31, 2019, there were an aggregate of 95,567 shares of common stock issuable upon the exercise of the warrants with a weighted-average exercise price of $6.80 per share. These instruments are included in the equity attributable to noncontrolling interests.

12. Income Taxes

As of December 31, 2019 and 2018, the Company had approximately $298.6 million and $249.6 million of federal net operating loss carryforwards and $13.6 million and $12.2 million of research tax credit carryforwards, respectively. The net operating loss carryforwards and research tax credit carryforwards begin to expire in 2031 and 2029, respectively. As of December 31, 2019 and 2018, the Company had foreign net operating loss carryforwards of approximately $99.3 million and $105.0 million, respectively. As of December 31, 2019 and 2018, the Company had state net operating losses of $262.5 million and $249.2 million, respectively.

Section 382 of the Internal Revenue Code of 1986, as amended (the "Code") provides for limitation on the use of net operating loss and research and development tax credit carryforwards following certain ownership changes (as defined in Code) that

could limit the Company's ability to utilize these carryforwards. Pursuant to Section 382 of the Code, an ownership change occurs when the stock ownership of a 5% stockholder increases by more than 50% over a three-year testing period. The Company may have experienced various ownership changes, as defined by the Code, as a result of past financing and may in the future experience an ownership change. Accordingly, the Company's ability to utilize the aforementioned carryforwards may be limited. Additionally, U.S. tax laws limit the time during which these carryfowards may be applied against future taxes.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provided guidance on accounting for the federal tax rate change and other tax effects of the Tax Cuts and Jobs Act (the "Tax Act"). SAB 118 provided a measurement period that should not extend beyond one year from the Tax Act enactment date for companies to complete the accounting under ASC 740, *Income Taxes*. In connection with the Company's adoption of the Tax Act and in consideration of SAB 118, there were no material adjustments made to the provisional amounts recognized in 2018 in connection with the enactment of the Tax Act. The accounting for the income tax effects of the Tax Act is complete as of December 31, 2018.

The components of the net deferred income tax asset as of December 31, 2019 and 2018 are as follows (amounts in thousands):

	December 31,	
	2019	2018
Deferred taxes:		
Net operating loss carryforwards	$ 96,378	$ 87,446
Research and development credit carryforwards	13,404	12,196
Stock-based compensation	4,107	5,209
Accruals	414	1,233
Right-of-use asset	(742)	—
Lease liability	934	—
Capitalized start-up costs	855	1,031
Other	10	936
Gross deferred tax asset	115,360	108,051
Less: valuation allowance	(115,360)	(108,051)
Net deferred tax asset	$ —	$ —

In assessing the realizability of deferred tax assets, the Company considers whether it is more-likely-than-not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which the temporary differences representing net future deductible amounts become deductible. After consideration of all the evidence, both positive and negative, the Company has recorded a full valuation allowance against its net deferred tax assets as of December 31, 2019 because the Company has determined that is it more likely than not that these assets will not be fully realized due to historic net operating losses incurred. The valuation allowance increased by $7.3 million during the year ended December 31, 2019, primarily due to the generation of net operating losses and credit carryforwards during 2019.

The Company does not have unrecognized tax benefits as of December 31, 2019 and 2018, respectively. The Company recognizes interest and penalties accrued on any unrecognized tax benefits as a component of income tax expense.

A reconciliation of income tax expense (benefit) at the statutory federal income tax rate and income taxes as reflected in the financial statements is as follows:

	December 31,	
	2019	2018
Federal income tax benefit at statutory rate	21.0 %	21.0 %
State income tax, net of federal benefit	2.4 %	4.1 %
Permanent differences	(1.0)%	(4.1)%
Rate change	(8.7)%	(3.3)%
Research and development credit benefit	2.7 %	5.0 %
Change in valuation allowance	(16.4)%	(22.7)%
Effective income tax rate	— %	— %

The Company files income tax returns in the U.S. Federal, various states and foreign jurisdictions. The statute of limitations for assessment by the Internal Revenue Service (IRS) and state tax authorities is open for the Company's 2016 to 2018 tax years. Federal and state carryforward attributes that were generated prior to the tax year ended December 31, 2016 may still be adjusted upon examination by the IRS or state tax authorities if they either have been or will be used in a period for which the statute of limitations remains open. The statute of limitations for assessment by the authorities in the various foreign jurisdictions in which the Company files ranges from one to five years and is open for the Company's 2016 to 2018 tax years. There are currently no federal, state or foreign income tax audits in progress.

13. Related Party Transactions

During the year ended December 31, 2018, the Company received $8 million upon issuing convertible promissory notes to several of its existing preferred stock investors. The notes were converted in December 2018 in connection with the Merger. The Company also received gross proceeds of $21.5 million from those same investors from the sale of common stock immediately prior to the Merger.

As discussed in Note 1, the Company sold shares of its common stock in December 2019. Roche invested in the Company's December 2019 financing. One of the Company's Board members is affiliated with Roche.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, 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, and that such information is accumulated and communicated to the company's management, including its chief executive officer and chief financial officer, 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.

Our management, with the participation of our chief executive officer and our chief financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2019. Based on the evaluation of our disclosure controls and procedures as of December 31, 2019, 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.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Our management, under the supervision and with the participation of our chief executive officer and our chief financial officer, conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2019 based on the framework in Internal Control-Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on the results of its evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2019. Our independent registered public accounting firm, Ernst & Young LLP, has audited our financial statements included in this Annual Report on Form 10-K and the effectiveness of our internal control over financial reporting as of December 31, 2019. The report of Ernst & Young LLP is incorporated by reference to Item 8 of this Annual Report on Form 10-K.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended December 31, 2019 which have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Our management, including our chief executive officer and our chief financial officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, have been detected. These inherent limitations include the realities that judgments in decision making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the controls. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Millendo Therapeutics, Inc.

Opinion on Internal Control Over Financial Reporting
We have audited Millendo Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2019, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Millendo Therapeutics, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, convertible preferred stock, redeemable noncontrolling interests and stockholders' (deficit) equity, and cash flows for each of the two years in the period ended December 31, 2019, and the related notes and our report dated March 11, 2020 expressed an unqualified opinion thereon.

Basis for Opinion
The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

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

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

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

/s/ Ernst & Young LLP

Grand Rapids, Michigan
March 11, 2020

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item is set forth in our proxy statement to be filed with respect to the 2020 annual meeting of shareholders (the "Proxy Statement"), all of which is incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is set forth in our Proxy Statement, all of which 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 is set forth in our Proxy Statement, all of which is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is set forth in our Proxy Statement, all of which is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item is set forth in our Proxy Statement, all of which is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

We have filed the following documents as part of this Annual Report:

(a)(1) Financial Statements

The financial statements are included in Item 8. "Financial Statements and Supplementary Data."

(a)(2) Financial Statement Schedules

All schedules are omitted as information required is inapplicable or the information is presented in the financial statements and the related notes.

(a)(3) Exhibits

Exhibit Number	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant, as amended (incorporated by reference from Exhibit 3.1 to the Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 15, 2019, File No. 001-35890)
3.2	Third Amended and Restated Bylaws, as Amended, of the Registrant (incorporated by reference from Exhibit 3.1 to the Current Report on Form 8-K filed with the Securities and Exchange Commission on August 9, 2018, File No. 001-35890)
4.1	Specimen Stock Certificate evidencing shares of Common Stock of the Registrant (incorporated by reference from Exhibit 4.1 to the Registration Statement on Form S-1 filed on August 29, 2012, File No. 333-183602)
4.6	Description of Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934
10.1+	OvaScience, Inc. 2011 Stock Incentive Plan (incorporated by reference from Exhibit 10.1 to the Registration Statement on Form 10 filed on April 11, 2012, File No. 000-54647)
10.2+	Form of Incentive Stock Option Agreement under the OvaScience, Inc. 2011 Stock Incentive Plan (incorporated by reference from Exhibit 10.2 to the Registration Statement on Form 10 filed on May 17, 2012, File No. 000-54647)
10.3+	Form of Nonstatutory Stock Option Agreement under the OvaScience, Inc. 2011 Stock Incentive Plan (incorporated by reference from Exhibit 10.3 to the Registration Statement on Form 10 filed on May 17, 2012, File No.000-54647)
10.4+	Form of Restricted Stock Agreement under the OvaScience, Inc. 2011 Stock Incentive Plan (incorporated by reference from Exhibit 10.4 to the Registration Statement on Form 10 filed on April 11, 2012, File No. 000-54647)
10.5+	OvaScience, Inc. 2012 Stock Incentive Plan (incorporated by reference from Exhibit 10.5 to the Registration Statement on Form 10 filed on April 11, 2012, File No. 000-54647)
10.6+	Form of Incentive Stock Option Agreement under the OvaScience, Inc. 2012 Stock Incentive Plan (incorporated by reference from Exhibit 10.6 to the Annual Report on Form 10-K filed on March 16, 2015, File No. 001-35890)
10.7+	Form of Nonstatutory Stock Option Agreement under the OvaScience, Inc. 2012 Stock Incentive Plan (incorporated by reference from Exhibit 10.7 to the Annual Report on Form 10-K filed on March 16, 2015, File No. 001-35890)
10.8+	Form of Inducement Nonqualified Stock Option Agreement subject to the terms of the OvaScience 2012 Stock Incentive Plan
10.9+	Millendo Therapeutics, Inc. 2012 Stock Incentive Plan, as amended (incorporated by reference from Exhibit 10.8 to the Annual Report on Form 10-K filed on April 1, 2019, File No. 001-35890)

10.10+	Form of Stock Option Agreement under the Millendo Therapeutics, Inc. 2012 Stock Incentive Plan (incorporated by reference from Exhibit 10.9 to the Annual Report on Form 10-K filed on April 1, 2019, File No. 001-35890)
10.11+	Sub Plan for French Residents to the Millendo Therapeutics, Inc. 2012 Stock Plan, as amended (incorporated by reference from Exhibit 10.5 to the Current Report on Form 8-K, as filed with the Securities and Exchange Commission on December 13, 2018, File No. 001-35890)
10.12+	Form of Stock Option Agreement under the Sub Plan for French Residents to the Millendo Therapeutics, Inc. 2012 Stock Plan, as amended (incorporated by reference from Exhibit 10.11 to the Annual Report on Form 10-K filed on April 1, 2019, File No. 001-35890)
10.13+	2019 Equity Incentive Plan (incorporated by reference from Exhibit 10.1 to the Current Report on Form 8-K filed with the Securities and Exchange Commission on June 13, 2019, File No. 001-35890)
10.14+	Form of Option Grant Package under 2019 Equity Incentive Plan (incorporated by reference from Exhibit 10.7 to the Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 12, 2019, File No. 001-35890)
10.15+	Form of RSU Grant Package under 2019 Equity Incentive Plan (incorporated by reference from Exhibit 10.8 to the Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 12, 2019, File No. 001-35890)
10.16+	Form of Stock Option Agreement under the Sub Plan for French Residents under 2019 Equity Incentive Plan
10.17+	Form of Inducement Nonqualified Stock Option Agreement subject to the terms of the 2019 Equity Incentive Plan
10.18+	2019 Employee Stock Purchase Plan (incorporated by reference from Exhibit 10.2 to the Current Report on Form 8-K filed with the Securities and Exchange Commission on June 13, 2019, File No. 001-35890)
10.19+	Form of Indemnity Agreement between Millendo Therapeutics, Inc. and each of its directors and executive officers (incorporated by reference from Exhibit 10.1 to the Current Report on Form 8-K, as filed with the Securities and Exchange Commission on December 13, 2018, File No. 001-35890)
10.20	Stock Purchase Agreement, by and among OvaScience, Inc., the purchasers set forth on Schedule I thereto and Millendo Therapeutics, Inc., dated November 1, 2018 (incorporated by reference from Exhibit 10.45 to the Registration Statement on Form S-4 filed on November 2, 2018, File No. 333-227547)
10.21	First Amendment to Shareholders and Option Agreement, dated September 28, 2018 (incorporated by reference from Exhibit 4.9 to the Registration Statement on Form S-3, as filed with the Securities and Exchange Commission on November 6, 2018, File No. 333-228209)
10.22	Registration Rights Agreement, by and among OvaScience, Inc. and the persons listed on Schedule A thereto, dated November 1, 2018 (incorporated by reference from Exhibit 10.46 to the Registration Statement on Form S-4 filed on November 2, 2018, File No. 333-227547)
10.23	Second Amended and Restated Investor Rights Agreement by and among Millendo Therapeutics, Inc. and certain of its stockholders, dated December 19, 2017 (incorporated by reference from Exhibit 4.6 to the Registration Statement on Form S-3, as filed with the Securities and Exchange Commission on November 6, 2018, File No. 333-228209)
10.24	First Amendment to Second Amended and Restated Investor Rights Agreement, dated October 24, 2018 (incorporated by reference from Exhibit 4.7 to the Registration Statement on Form S-3, as filed with the Securities and Exchange Commission on November 6, 2018, File No. 333-228209)
10.25	Shareholders and Option Agreement, by and between Millendo Therapeutics, Inc. and Otonnale SAS, dated December 19, 2017 (incorporated by reference from Exhibit 4.8 to the Registration Statement on Form S-3, as filed with the Securities and Exchange Commission on November 6, 2018, File No. 333-228209)
10.26	Amended and Restated Equity Distribution Agreement dated March 4, 2020, between Millendo Therapeutics, Inc., Citigroup Global Markets Inc. and SVB Leerink LLC (incorporated by reference from Exhibit 1.1 to the Current Report on Form 8-K filed with the Securities and Exchange Commission on March 4, 2020, File No. 333-230749)
10.27	Lease Agreement, by and between Millendo Therapeutics, Inc. and 301 N. Main Street, L.L.C., dated December 31, 2015 (incorporated by reference from Exhibit 10.1 to the Registration Statement on Form S-3, as filed with the Securities and Exchange Commission on November 6, 2018, File No. 333-228209)

10.28	Lease Extension and Modification Agreement, by and between Millendo Therapeutics, Inc. and 301 N. Main Street, L.L.C., dated November 30, 2017 (incorporated by reference from Exhibit 10.2 to the Registration Statement on Form S-3, as filed with the Securities and Exchange Commission on November 6, 2018, File No. 333-228209)
10.29	Lease Agreement, by and between Millendo Therapeutics, Inc. and Ann Arbor Real Estate Group, L.L.C., dated October 22, 2018
10.30	Sublease Agreement by and between OvaScience, Inc. and Axial Biotherapeutics, Inc., dated as of December 6, 2018 (incorporated by reference from Exhibit 10.1 to the Current Report on Form 8-K, as filed with the Securities and Exchange Commission on December 13, 2018, File No. 001-35890)
10.31	Lease Agreement, by and between Millendo Therapeutics, Inc. and Ann Arbor Real Estate Group, L.L.C., dated February 1, 2019 (incorporated by reference from Exhibit 10.1 to the Current Report on Form 8-K, as filed with the Securities and Exchange Commission on February 7, 2019, File No. 001-35890)
10.32	Amended and Restated Lease Extension and Modification Agreement, by and between Millendo Therapeutics, Inc. and 301 N. Main Street, L.L.C., dated February 1, 2019 (incorporated by reference from Exhibit 10.2 to the Current Report on Form 8-K, as filed with the Securities and Exchange Commission on February 7, 2019, File No. 001-35890)
10.33	Flex Space Agreement, dated April 11, 2019 (incorporated by reference from Exhibit 10.1 to the Current Report on Form 8-K filed with the Securities and Exchange Commission on April 17, 2019, File No. 001-35890)
10.34#	Amended and Restated License Agreement, by and between Millendo Therapeutics, Inc. and the Regents of the University of Michigan, dated November 9, 2015 (incorporated by reference from Exhibit 10.44 to the Registration Statement on Form S-4 filed on November 2, 2018, File No. 333-227547)
10.35#	License Agreement, by and among F. Hoffmann-La Roche Ltd, Hoffman-La Roche Inc. and Millendo Therapeutics, Inc., dated October 16, 2018 (incorporated by reference from Exhibit 10.4 to the Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 12, 2019 File No. 001-35890)
10.36	Assignment Agreement, by and among Alizé Pharma SAS (n/k/a Millendo Therapeutics SAS), Erasmus University Medical Center and the University of Turin, dated April 25, 2007 (incorporated by reference from Exhibit 10.51 to the Registration Statement on Form S-4 filed on November 2, 2018, File No. 333-227547)
10.37	Contract No. A1308020, by and between Alizé Pharma SAS (n/k/a Millendo Therapeutics SAS) and Bpifrance Financement, dated January 27, 2014 (incorporated by reference from Exhibit 10.47 to the Registration Statement on Form S-4 filed on November 2, 2018, File No. 333-227547)
10.38	Contract No. A1308020, by and between Alizé Pharma SAS (n/k/a Millendo Therapeutics SAS) and Bpifrance Financement, dated January 27, 2014 (English Translation) (incorporated by reference from Exhibit 10.48 to the Registration Statement on Form S-4 filed on November 2, 2018, File No. 333-227547)
10.39+	Amended and Restated Employment Agreement, by and between Millendo Therapeutics US, Inc. and Julia C. Owens, Ph.D., dated June 7, 2019 (incorporated by reference from Exhibit 10.1 to the Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 12, 2019 File No., 001-35890)
10.40+	Employment Agreement, by and between Millendo Therapeutics US, Inc. and Tamara Joseph, dated July 11, 2019 (incorporated by reference from Exhibit 10.2 to the Quarterly Report on Form 10-Q filed on November 13, 2019, File No. 001-35890)
10.41+	Amended and Restated Employment Agreement, by and between Millendo Therapeutics US, Inc. and Ryan Zeidan, dated August 16, 2019 (incorporated by reference from Exhibit 10.1 to the Quarterly Report on Form 10-Q filed on November 13, 2019, File No. 001-35890)
10.42+	Amended and Restated Employment Agreement between Louis Arcudi III and Millendo Therapeutics US, Inc., dated as of June 19, 2019 (incorporated by reference from Exhibit 10.2 to the Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on August 12, 2019, File No. 001-35890)
10.43+	Employment Agreement between Christophe Arbet-Engels and Millendo Therapeutics US, Inc., dated as of February 5, 2020
21.1	Subsidiaries of the Registrant.
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm

24.1	Power of Attorney (included on signature page)
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to section 302 of the Sarbanes-Oxley Act of 2002
32.1^	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Rules 13a-14(b) and 15d-14(b) promulgated under the Securities Exchange Act of 1934 and 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 Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

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+ Indicates management contract or compensatory plan.

Confidential treatment has been granted with respect to portions of this exhibit (indicated by asterisks) and those portions have been separately filed with the Securities and Exchange Commission.

^ These certifications are being furnished solely to accompany this Annual Report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

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.

MILLENDO THERAPEUTICS, INC.

By: */s/ Julia C. Owens, Ph.D.*
Julia C. Owens, Ph.D.
President and Chief Executive Officer

March 11, 2020

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Julia C. Owens and Louis Arcudi III, jointly and severally, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign this Annual Report on Form 10-K of Millendo Therapeutics, Inc., and any or all amendments thereto, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his, her or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Julia C. Owens, Ph.D. Julia C. Owens, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 11, 2020
/s/ Louis Arcudi III Louis Arcudi III	Chief Financial Officer *(Principal Financial Officer and Principal Accounting Officer)*	March 11, 2020
/s/ Carol Gallagher, Pharm.D. Carol Gallagher, Pharm.D.	Chairperson of the Board of Directors	March 11, 2020
/s/ Habib Dable Habib Dable	Director	March 11, 2020
/s/ Mary Lynne Hedley, Ph.D. Mary Lynne Hedley, Ph.D.	Director	March 11, 2020
/s/ James Hindman James Hindman	Director	March 11, 2020
/s/ John P. Howe, III, M.D. John P. Howe, III, M.D.	Director	March 11, 2020
/s/ Geoff Nichol, M.B., Ch.B., M.B.A. Geoff Nichol, M.B., Ch.B., M.B.A.	Director	March 11, 2020
/s/ Carole Nuechterlein, J.D. Carole Nuechterlein, J.D.	Director	March 11, 2020

Board of Directors

Carol Gallagher, Pharm.D., Chairperson
Partner, New Enterprise Associates

Habib J. Dable
President and Chief Executive Officer, Acceleron Pharma

Mary Lynne Hedley, Ph.D.
President and Chief Operating Officer, TESARO

James M. Hindman
Former Executive Vice President and Chief Financial Officer, Allergan

John P. Howe III, M.D.
Former President and Chief Executive Officer of Project HOPE

Geoff Nichol, M.B., Ch.B., M.B.A.
Chief Medical Officer, BioMarin

Carole L. Nuechterlein, J.D.
Deputy Director and Head, Roche Venture Fund at F. Hoffmann-La Roche

Julia C. Owens, Ph.D.
President and Chief Executive Officer, Millendo Therapeutics

Leadership Team

Julia C. Owens, Ph.D.
President and Chief Executive Officer

Christophe Arbet-Engels, M.D., Ph.D.
Chief Medical Officer

Louis J. Arcudi III
Chief Financial Officer

Tamara Joseph
General Counsel

Ryan Zeidan, Ph.D.
Chief Development Officer

Thomas Hoover
Chief Commercial Officer

Corporate Headquarters

Millendo Therapeutics, Inc.
110 Miller Avenue, Suite 100
Ann Arbor, MI 48104

Legal Counsel

Cooley LLP
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