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

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2016
or

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

Commission File Number 001-36193

Trevena, Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**26-1469215**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
1018 West 8th Avenue, Suite A, King of Prussia, PA	**19406**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: **(610) 354-8840**

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

Title of each class	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	NASDAQ Global Select Market

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

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

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

Large accelerated filer ☐	Accelerated filer ☒	Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐

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 stock held by non-affiliates of the registrant, as of June 30, 2016, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $218.2 million. Such aggregate market value was computed by reference to the closing price of the Common Stock as reported on the NASDAQ Global Select Market on June 30, 2016. For purposes of making this calculation only, the registrant has defined affiliates as including only directors and executive officers and shareholders holding greater than 10% of the voting stock of the registrant as of June 30, 2016.

The number of shares of the registrant's Common Stock outstanding as of March 3, 2017 was 57,129,584.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2017 annual meeting of stockholders to be filed pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2016 are incorporated by reference into Part III of this Form 10-K.

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Cautionary Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K (this "Annual Report") contains forward-looking statements that involve substantial risks and uncertainties. The forward-looking statements are contained principally in the sections entitled "Business," "Risk Factors," and "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 potentially commercialize our product candidates;
- our ability to fund future operating expenses and capital expenditures with our current cash resources;
- our planned clinical trials and preclinical studies for our product candidates;
- the timing and likelihood of obtaining and maintaining regulatory approvals for our product candidates;
- the extent of clinical trials potentially required by the FDA for our product candidates;
- the clinical utility and market acceptance of our product candidates, particularly in light of existing and future competition;
- our commercialization, marketing and manufacturing capabilities and strategies;
- our intellectual property position; and
- our ability to identify additional product candidates with significant commercial potential that are consistent with our commercial objectives.

You should refer to the "Risk Factors" section of 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. 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.

PART I

ITEM 1. BUSINESS

Overview

Trevena, Inc. is a biopharmaceutical company developing innovative therapies based on breakthrough science to benefit patients and healthcare providers confronting serious medical conditions. Unless the context otherwise requires, we use the terms "Trevena," "company," "we," "us" and "our" to refer to Trevena, Inc.

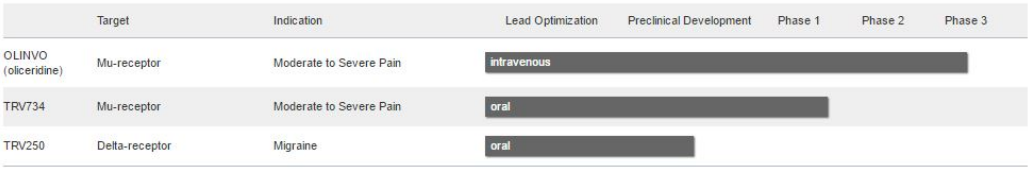
Using our proprietary product platform, we have identified and are developing the following product candidates:

- *OLINVO™ (oliceridine injection):* We are developing OLINVO, a μ-receptor G protein pathway selective modulator (μ-GPS), for the management of moderate-to-severe acute pain where intravenous, or IV, administration is preferred. On February 21, 2017, we announced positive top-line results from our Phase 3 APOLLO-1 and APOLLO-2 pivotal efficacy studies of OLINVO in moderate-to-severe acute pain following bunionectomy and abdominoplasty, respectively. In both studies, all dose regimens achieved their primary endpoint of statistically greater analgesic efficacy than placebo, as measured by responder rate. The Phase 3 open-label ATHENA-1 safety study commenced in January 2016 and more than 400 patients have been treated in this study as of February 15, 2017. We have retained all worldwide development and commercialization rights to OLINVO, and plan to commercialize it in the United States for use in acute care settings such as hospitals and ambulatory surgery centers if it receives regulatory approval.

- *TRV250:* We are developing TRV250, a G protein biased ligand targeting the δ-receptor, as a compound with a potential first-in-class, non-narcotic mechanism for the treatment of migraine. TRV250 also may have utility in a range of other central nervous system, or CNS, indications. Because TRV250 selectively targets the δ-receptor, we believe it will not have the addiction liability of conventional opioids or other μ-opioid related adverse effects like those seen with morphine or oxycodone. In the second quarter of 2017, we expect to commence a Phase I study of TRV250 in the United Kingdom in healthy volunteers.

In addition to the above product candidates, we identified and have completed the initial Phase 1 studies for TRV734, an orally administered new chemical entity expected to be used for first-line treatment of moderate-to-severe acute and chronic pain. We intend to continue to focus our efforts for TRV734 on securing a development and commercialization partner for this asset. We had also been developing TRV027 for the treatment of acute heart failure, or AHF. In May 2016, we announced that TRV027 did not meet either the primary or secondary endpoints of our Phase 2b (BLAST-AHF) clinical trial of the compound. In August 2016, Allergan plc (formerly Actavis plc and Forest Laboratories Holdings Limited), or Allergan, notified us of its decision to not exercise its exclusive option to license TRV027. We are seeking a partner to fund any future clinical testing of TRV027.

Our Pipeline



OLINVO™ (oliceridine injection)

OLINVO is a novel μ-receptor G protein Pathway Selective modulator that activates the G protein pathway, which is associated with analgesia and avoids the β-arrestin pathway, which is associated with limiting opioid analgesia and with promoting opioid-induced adverse events.We are developing OLINVO for the management of moderate-to- severe acute pain where IV administration is preferred.

Disease and treatment options

According to 2015 IMS data, approximately 51 million patients in the United States were treated with an IV opioid in the hospital setting. The majority of use is in the inpatient setting where approximately 16 million patients were treated an average of two days. In the outpatient setting, approximately 35 million patients were treated for an average of two hours. The World Health Organization estimates that over 230 million major surgical procedures are performed each year worldwide. The Centers for Disease Control and Prevention, or CDC, estimates that 100 million surgical and invasive diagnostic procedures occur annually in the United States. Based on market research, we believe that approximately 19 million hospital inpatient surgeries are performed collectively in France, Germany, the United Kingdom, Italy, and Spain each year. Accordingly, if approved, we believe that there is a large potential commercial opportunity for OLINVO in the management of both surgical and medical acute pain.

The typical treatment paradigm in developed markets for the management of moderate-to-severe acute pain is to initiate injectable or IV pain medication in the preoperative or immediate postoperative period to provide rapid and effective pain relief. Conventional IV opioid analgesics such as morphine, fentanyl and hydromorphone are the mainstays of pain management in the immediate postoperative period and are approximately 50% of the injectable analgesic unit market. In a 2012 survey of 300 surgical patients in the United States, over 80% of patients reported postoperative pain after the first analgesic medication had been administered, and 40% of this pain was reported to be moderate or severe. In addition, the effectiveness of conventional opioid agonists is limited because of severe side effects such as respiratory depression, nausea, vomiting, and constipation. Injectable non-opioid analgesics are often used together with IV opioids for post-surgical pain management; however, these drugs, such as IV non-steroidal anti-inflammatory drugs, or NSAIDs, IV acetaminophen or local anesthetics such as bupivacaine, have potential cardiovascular, hepatic and gastrointestinal side effects. None of these non-opioid analgesic approaches has displaced the use of opioid analgesics as the cornerstone of IV therapy for acute moderate-to-severe pain. We believe that there remains significant unmet need for an effective analgesic agent with an improved safety and tolerability profile.

Clinical development

In December 2015, the U.S. Food and Drug Administration, or FDA, granted Fast Track designation to OLINVO for the management of moderate-to-severe acute pain. The Fast Track program is designed to facilitate the development and review of drugs intended to treat serious conditions with unmet medical needs by providing sponsors with the opportunity for frequent interactions with the FDA. In February 2016, the FDA granted Breakthrough Therapy designation to OLINVO for the management of moderate-to-severe acute pain. Breakthrough Therapy designation is granted by the FDA to new therapies intended to treat serious conditions and for which preliminary clinical evidence indicates that the drug may demonstrate substantial clinical improvement over available therapies. Breakthrough Therapy designation provides all the benefits of the Fast Track program, as well as more intensive FDA guidance on preparing an efficient drug development program and eligibility for rolling review and priority review. We currently expect to submit a new drug application, or NDA, for OLINVO in the fourth quarter of 2017.

We are developing OLINVO for the management of moderate-to-severe acute pain where IV administration is preferred. In the future, we also may explore other formulations, such as transmucosal or transdermal administration for breakthrough or chronic pain, respectively, in additional, separate clinical trials.

Phase 3 development program

In January 2016, we initiated the Phase 3 clinical program for OLINVO with the enrollment of patients in the ATHENA study, a Phase 3, open label, multicenter study evaluating the safety and tolerability of OLINVO in approximately 900 patients. The study is enrolling eligible patients with moderate-to-severe pain caused by medical conditions or surgery. Patients are treated with OLINVO on an as-needed basis via IV bolus, patient-controlled analgesia, or PCA, or both, as determined by the investigator. The primary objective is to assess the safety and tolerability of OLINVO. Pain intensity is being measured as a secondary endpoint. As of February 15, 2017, over 400 patients have been treated in the ATHENA study, with no apparent off-target or unexpected adverse effects.

In the first quarter of 2016, we discussed our Phase 3 development program with the FDA at an End of Phase 2 meeting. At this meeting, the FDA agreed that pivotal efficacy trials in bunionectomy and abdominoplasty patients include appropriate patient populations to support an indication for the management of moderate-to-severe acute pain.

The FDA also confirmed the need for at least 1,100 patients exposed to OLINVO across the development program for the purposes of evaluating safety and tolerability and that the trials should include a sufficient number of patients with higher exposures and longer durations of OLINVO therapy. In addition, general agreement was reached on our planned clinical, nonclinical, clinical pharmacology, and chemistry, manufacturing and control activities to support the planned NDA.

APOLLO-1 and APOLLO-2 Phase 3 Studies

In the second quarter of 2016, we commenced two pivotal efficacy trials evaluating OLINVO in patients with moderate-to-severe acute pain: the APOLLO-1 study, which evaluated pain for 48 hours following bunionectomy, and the APOLLO-2 study, which evaluated pain for 24 hours following abdominoplasty. On February 21, 2017, we announced positive top-line results from the APOLLO-1 and APOLLO-2 studies. In both studies, all dose regimens achieved the primary endpoint of statistically greater analgesic efficacy than placebo, as measured by responder rate.

The APOLLO-1 and APOLLO-2 studies were both Phase 3, multicenter, randomized, double-blind, placebo- and active-controlled studies of OLINVO. During the study period, a loading dose of placebo, morphine (4 mg), or OLINVO (1.5 mg) was administered first, and then patients used a PCA button to dose themselves as often as every 6 minutes with the same study drug: 1 mg morphine or 0.1 mg, 0.35 mg, or 0.5 mg OLINVO. If PCA dosing was inadequate to control pain, patients could request supplemental study medication (0.75 mg OLINVO or 2 mg morphine, no more than once an hour). If the study medication regimen did not adequately manage pain, patients could opt for an NSAID rescue analgesic. Placebo loading, demand, and supplemental doses were volume-matched.

All endpoints were the same in both studies. Efficacy was measured by a responder analysis, which defined a responder as a patient who experienced at least a 30% reduction in their sum of pain intensity difference at the end of the treatment period without either early discontinuation (for lack of efficacy or safety/tolerability) or use of rescue medication. Non-inferiority to morphine and superiority to morphine were key secondary endpoints. Respiratory safety events were defined as clinically relevant worsening of respiratory status, including oxygen saturation, respiratory rate, or sedation. The product of the frequency and conditional duration of these events was reported as respiratory safety burden, a key secondary endpoint. Additional measures of respiratory safety included prevalence of oxygen saturation less than 90% and prevalence of supplemental oxygen use. Measures of gastrointestinal tolerability included use of rescue antiemetics, vomiting, and spontaneously reported nausea.

APOLLO-1 (bunionectomy)

- All three OLINVO regimens (0.1 mg, 0.35 mg, and 0.5 mg on-demand doses) achieved the primary endpoint with statistically superior responder rates compared to placebo at 48 hours ($p<0.0001$, adjusted for multiplicity).
- The 0.35 mg and 0.5 mg OLINVO dose regimens demonstrated efficacy comparable to morphine at 48 hours based on responder rate (both doses $p<0.005$ for non-inferiority to morphine). Both doses were also comparable to morphine for rates of rescue analgesic use.
- Following the 1.5 mg initial loading dose, all OLINVO regimens demonstrated rapid onset with statistically significant efficacy by 5 minutes ($p<0.05$).
- OLINVO exhibited a dose-related trend of improved respiratory safety burden in all three OLINVO dose regimens ($p<0.05$ for the 0.1 mg regimen vs. morphine). Consistent with this, in all dose regimens OLINVO showed dose-related trends of reduced prevalence of oxygen desaturation ($O_2<90\%$) and lower prevalence of supplemental oxygen use ($p<0.05$ for the 0.1 mg regimen vs. morphine for both measures).
- OLINVO exhibited a dose-related trend of less antiemetic use compared to morphine ($p<0.05$ for all OLINVO regimens vs. morphine). Consistent with this, OLINVO showed dose related trends of lower prevalence of nausea and vomiting in all three OLINVO regimens ($p<0.05$ for the 0.1 mg regimen vs. morphine).

APOLLO-2 (abdominoplasty)

- All three OLINVO dose regimens achieved the primary endpoint with statistically superior responder rates compared to placebo (adjusted $p<0.05$ for the 0.1 mg regimen; adjusted $p<0.001$ for the 0.35 mg and 0.5 mg regimens).
- The 0.35 mg and 0.5 mg OLINVO dose regimens demonstrated efficacy comparable to morphine at 24 hours based on responder rate ($p<0.05$ for non-inferiority of the 0.35 mg regimen vs. morphine). Both doses were also comparable to morphine for rates of rescue analgesic use.
- Following the 1.5 mg initial loading dose, all OLINVO regimens demonstrated rapid onset with statistically significant efficacy by 5 to 15 minutes ($p<0.05$).
- OLINVO showed a dose-related trend of improved respiratory safety burden in all three OLINVO dose regimens ($p<0.05$ for the 0.1 mg regimen vs. morphine). Consistent with this, for all dose regimens OLINVO showed dose-related trends of reduced prevalence of oxygen desaturation ($O_2<90\%$) and lower prevalence of supplemental oxygen use ($p<0.05$ for the 0.1 mg regimen vs. morphine for both measures).
- OLINVO showed a dose-related trend of less antiemetic use than morphine for all three OLINVO regimens ($p<0.05$ for the 0.1 mg OLINVO regimen vs. morphine). Consistent with this, OLINVO showed dose-related trends of lower prevalence of nausea and vomiting ($p<0.05$ for the 0.1 mg regimen vs. morphine for both nausea and vomiting; $p<0.05$ for the 0.35 mg regimen vs. morphine for vomiting).

In both studies, oliceridine was generally well-tolerated. The most common drug-related adverse events were nausea, vomiting, headache, and dizziness.

Phase 2b trial of OLINVO in acute postoperative pain following abdominoplasty

The aim of our Phase 2b clinical trial was to evaluate the efficacy, safety and tolerability of OLINVO in the management of postoperative pain using morphine as a benchmark, utilizing on-demand dosing to reflect standard clinical practice. This Phase 2b trial was a randomized, double-blind, placebo- and active-controlled trial of OLINVO in which we enrolled 200 patients with moderate-to-severe acute postoperative pain after abdominoplasty surgery. Two regimens of OLINVO were tested: the first consisted of a 1.5 mg intravenous loading dose with 0.1 mg self-administered on-demand doses as often as every six minutes using a PCA device; the second consisted of a 1.5 mg loading dose with 0.35 mg on-demand doses as often as every six minutes using a PCA device. A commonly used morphine PCA regimen also was tested, consisting of a 4 mg loading dose with 1 mg on-demand doses as often as every six minutes. Placebo was administered as a loading dose and on-demand doses were volume-matched to the active regimens. Rescue medication consisting of ibuprofen or oxycodone was used in all groups.

In August 2015, we reported top-line results from this trial. OLINVO demonstrated statistically significant pain reduction compared to placebo and comparable efficacy to morphine. OLINVO provided rapid reduction in average pain scores, consistent with the previous Phase 2 trial where OLINVO showed more rapid onset of meaningful pain relief than morphine. Rescue analgesic use was similar for both OLINVO and morphine, and less than half the rate of rescue analgesic use for placebo. In this study, the OLINVO groups had a significantly lower prevalence (percentage of patients) of hypoventilation events (a measure of respiratory safety), nausea, and vomiting than the morphine group. The most frequently reported adverse events, or AEs, associated with OLINVO were nausea, vomiting, hypoventilation and headache. Opioid-related AEs were generally less frequent in the OLINVO groups compared to morphine. No drug-related serious adverse events were reported in the study.

Phase 2a/b trial of OLINVO in acute postoperative pain following bunionectomy

The aim of our Phase 2a/b clinical trial was to evaluate the efficacy and tolerability of OLINVO in the management of postoperative pain using morphine as a benchmark, using fixed dose and dose interval to characterize the performance of OLINVO. The trial was a multicenter, randomized, double-blind, placebo- and active-controlled, multiple dose, adaptive trial in 333 women and men undergoing a primary unilateral first-metatarsal bunionectomy surgery at four sites in the United States. Patients were randomized after surgery to receive OLINVO, morphine or placebo to manage their pain. Pain intensity was measured using validated numeric rating scales ranging from ten (most severe pain) to zero (no pain) at multiple time points up to 48 hours. Based on these scales, analgesic efficacy was

assessed with a time-weighted average change in pain score over 48 hours—a well-established measure of changes in the intensity of pain over time and an FDA-recommended endpoint for pain studies.

In November 2014, we announced top-line data from this trial. At doses of 2 mg and 3 mg of OLINVO administered every three hours, the trial achieved its primary endpoint of statistically greater pain reduction than placebo for 48 hours, which we believe demonstrates proof of concept for OLINVO. Over the 48-hour trial period, the 3 mg dose of OLINVO administered every three hours also showed statistically superior analgesic efficacy compared to the 4 mg dose of morphine administered every four hours. Additionally, in the first three hours of dosing, when pain was most severe, the 1 mg, 2 mg and 3 mg doses of OLINVO demonstrated superior analgesic efficacy in the trial compared to placebo, and the 2 mg and 3 mg doses of OLINVO demonstrated superior analgesic efficacy compared to the 4 mg dose of morphine.

There were no serious adverse events reported in the trial. Both the 2 mg and 3 mg doses of OLINVO showed overall tolerability over the 48-hour trial period similar to that of the 4 mg dose of morphine administered every four hours. The most frequently reported adverse events associated with OLINVO were dizziness, headache, somnolence, nausea, vomiting, flushing and itching. Adverse effects were generally dose-related.

Phase 1 clinical studies of OLINVO

We have completed a number of Phase 1 clinical studies of OLINVO. These included two single ascending dose studies of OLINVO given as a 60 minute continuous infusion or a 2 minute bolus infusion that showed dose-related increases in plasma exposure and pupil constriction, a biomarker for CNS opioid activity across a range of doses that were generally well tolerated. Because in vitro data suggest that OLINVO is metabolized by at least two liver enzymes, CYP2D6 and CYP3A4, we assessed OLINVO pharmacokinetics, pharmacodynamics, safety and tolerability in CYP2D6 “poor metabolizer” healthy volunteers with little to no CYP2D6 activity. This study showed that OLINVO clearance was reduced by approximately 50% in the poor metabolizers suggesting that a lower frequency of dosing may be required to offer effective pain relief.

In 2013, we completed a Phase 1b proof of concept exploratory trial in healthy male subjects. The aims of this trial were to characterize the analgesic efficacy and safety and tolerability of a single dose of OLINVO as compared to a single 10 mg dose of morphine. We used a well-established evoked-pain model, the cold pain test, to evaluate the analgesic effects of OLINVO by measuring the time to hand removal, or latency, from a temperature-controlled cold water bath. At both the 3.0 mg and 4.5 mg doses, OLINVO showed superior efficacy as compared to a 10 mg morphine dose that was statistically significant with a p-value of less than 0.05 at the ten and 30 minute time points after dosing. The durability of the analgesic effect was similar to morphine. In addition, the time to peak effect was more rapid than that for morphine. Overall, OLINVO was well tolerated in the trial. Subjects receiving OLINVO showed less severe nausea and less frequent vomiting at the 1.5 mg and 3.0 mg doses as compared to a 10 mg dose of morphine. OLINVO also showed less respiratory depression compared to morphine over 4 hours.

In October 2014, we completed an adaptive, multiple ascending dose study of OLINVO in more than 50 healthy subjects. The safety, tolerability, pharmacokinetics and pharmacodynamics results of this study were consistent with the earlier Phase 1 studies described above. Recently, we also successfully completed an absorption, distribution, metabolism, and excretion study, a QTc interval study, a renal impairment study, and a human abuse liability study.

Commercialization

We intend to build hospital commercial capabilities in the United States and retain full U.S. rights to OLINVO. We expect to seek collaborators to commercialize OLINVO outside the United States to offset risk and preserve capital.

To commercialize OLINVO in the United States, we intend to utilize a hospital-focused specialty sales force targeting surgeons, anesthesiologists, hospitalists, and other healthcare providers with acute post-surgical or medical pain management responsibility. Within the inpatient setting, we believe that there will be opportunities for OLINVO in the post-anesthesia care unit, the emergency department, the intensive/critical care unit, and the medical/surgical floor. Based on market research conducted to date with key customers, we currently expect to focus on multiple surgical and medical procedures in which OLINVO may be a good clinical fit due to patient or procedure characteristics. In targeted hospitals, we will work to secure Pharmacy and Therapeutics Committee approval and subsequent pull-through utilization of OLINVO. Given the changing dynamics in the hospital marketplace and the increased emphasis on clinical

and economic outcomes, we expect our commercialization plans also will include health economic information designed to demonstrate the value OLINVO could provide to the healthcare system through a potential reduction in adverse events related to the use of conventional IV opioids. Because many of our targeted customers also provide care in other hospital settings, we anticipate that we will also target a select number of hospital outpatient departments and ambulatory surgery centers.

Manufacturing

We have completed process development of the active pharmaceutical ingredient, or API, and have manufactured multiple commercial scale batches using our proposed commercial process under commercial good manufacturing practices, or cGMP, conditions. We also have completed drug product process development and have manufactured multiple batches of drug product using the proposed commercial process under cGMP conditions. Both API and drug product will be manufactured in the United States by third party contract manufacturing vendors with which we have established contractual relationships for supply.

Competition

If OLINVO is approved for IV management of moderate-to-severe acute pain, it will compete with generic IV opioid analgesics, such as morphine, hydromorphone and fentanyl. The analgesic effectiveness of these agents is limited by well-known adverse side effects, such as respiratory depression, nausea, vomiting, constipation, and post-operative ileus. OLINVO also may compete against, or be used in combination with, OFIRMEV® (IV acetaminophen), marketed by Mallinckrodt plc, with EXPAREL® (liposomal bupivacaine), marketed by Pacira Pharmaceuticals, Inc., CALDOLOR® (IV ibuprofen), marketed by Cumberland Pharmaceuticals, DYLOJECT™ (IV diclofenac), marketed by Pfizer Inc., and IONSYS® marketed by The Medicines Company. Together with generic versions of IV NSAIDs such as ketorolac, and generic versions of local anesthetics such as bupivacaine, these non-opioid analgesics are currently used in combination with opioids in the multimodal management of moderate-to-severe acute pain.

We also are aware of a number of products in mid- and late-stage clinical development that are aimed at improving the treatment of moderate-to-severe, acute pain and will directly compete with OLINVO. AcelRx Pharmaceuticals, Inc. is developing a range of acute pain products involving sufentanil oral nanotabs in hand-held dispensers including DSUVIA™ and ZALVISO™. Durect Corporation, Innocoll Holdings plc, and Heron Therapeutics Inc. all have proprietary long-acting reformulations of bupivacaine in development. Recro Pharma, Inc. is developing an IV version of the NSAID meloxicam. Cara Therapeutics Inc. is developing IV and oral dose forms of a peripherally restricted κ-opioid receptor agonist, which has been administered in combination with μ-opioids in clinical trials.

Intellectual property

Our OLINVO patent portfolio is wholly owned by us. The portfolio includes two issued U.S. patents (U.S. Patent Nos. 8,835,488 and 9,309,234), which claim among other things, OLINVO, compositions comprising OLINVO and methods of using OLINVO. The portfolio also includes one allowed U.S. patent application (U.S. Patent Application No. 15/093,315) claiming OLINVO, other compounds and/or methods of making or using the same. The issued patents are expected to expire no earlier than 2032, subject to any disclaimers or extensions and any U.S. patent to issue in the future is also expected to expire no earlier than 2032, subject to any disclaimers or extensions. We also have issued patents in Japan and New Zealand, which claim among other things, OLINVO, compositions comprising OLINVO and methods of using OLINVO. The foreign portfolio also includes applications that have been allowed in China, Australia and by the European Patent Office, which claim among other things, OLINVO, compositions comprising OLINVO and methods of using OLINVO. We have patent applications pending in South Korea, the European Patent Office, the Eurasian Patent Office, Australia, Brazil, Canada, Israel, India, Japan, China, Hong Kong and New Zealand. The issued patents and patents that could issue in the future from these allowed or pending applications outside the United States are expected to expire no earlier than 2032, subject to any disclaimers or extensions.

TRV250

TRV250 is a small molecule G protein biased ligand of the δ-opioid receptor in preclinical development. In the second quarter of 2017, we expect to commence a Phase I study of TRV250 in the United Kingdom in healthy volunteers. Based on the profile of TRV250, we believe it has the potential to be a first-in-class treatment for migraine. According to Decision Resources, a healthcare consulting company, the acute episodic migraine market encompassed

approximately 12 million drug-treated patients in 2013 in the United States, representing approximately $2.2 billion of sales. We estimate that approximately 20% to 30% of these patients either do not respond to or cannot tolerate the market-leading triptan drug class, and an additional 30% would benefit from improved efficacy compared to these drugs.

Triptans, a generic family of $5HT_{1B}$ agonists, are the current standard treatment for acute treatment of migraine, and account for 80% of migraine therapies prescribed during physician office visits. Other less commonly prescribed acute treatments include ergot alkaloids, and analgesics such as opioids and NSAIDs. Various branded reformulations of triptan molecules have been launched and we are aware of others in development. In May 2016, Avanir Pharmaceuticals, Inc. launched a dry powder nasal delivery formulation of sumatriptan, called ONZETRA™ Xsail™. RedHill Biopharma, Ltd. and IntelGenx Corp. plan to resubmit the NDA for RIZAPORT ®, an oral thin film rizatriptan formulation, to the FDA in the first half of 2017. In addition, Allergan is developing an orally inhaled formulation of dihydroergotamine, called Semprana™. Lasmiditan, an selective $5HT_{1F}$ agonist, is in late stage development by Colucid Pharmaceuticals, Inc., recently acquired by Eli Lilly and Company. Allergan also has an oral anti-calcitonin gene-related peptide, or CGRP, ubrogepant (MK-1602), in Phase 3 testing for the acute treatment of migraine.

Patients suffering from frequent or chronic migraine headaches may also use preventative agents to decrease the frequency and severity of migraines. Botox® is currently the most widely prescribed migraine prophylactic, but certain anticonvulsants, such as topiramate, and beta-blockers, such as propranolol, are also used. We are aware of four companies with anti-CGRP antibodies in mid-to-late stage development for preventative treatment of migraine: Amgen, Inc. with AMG 334; Alder BioPharmaceuticals Inc. with ALD403; Eli Lilly and Company with LY2951742 and Teva Pharmaceutical Industries Limited with LBR-101.

We believe our preclinical data support targeting the δ-opioid receptor for the treatment of CNS disorders. Prior approaches to modulate this receptor have been limited by a significant risk of seizure associated with this target. By contrast, TRV250 is a potent δ-opioid receptor ligand that displayed strong efficacy in animal models of migraine and other CNS disorders with reduced seizure liability through selectively activating G protein coupling without engaging β-arrestin. These *in vivo* data are further supported by data for δ-agonists in β-arrestin knockout mice suggesting that β-arrestin plays a role in seizures. In the future, we may decide to seek a collaborator for TRV250 with CNS development and commercialization expertise outside the United States. Phase 1 clinical trials could include electroencephalogram studies to specifically assess seizure liability.

We have one non-provisional patent application in the United States directed to compounds that modulate the δ-opioid receptor. This application is solely owned by us. We have also filed a Patent Cooperation Treaty, or PCT, application and anticipate filing foreign national phase applications based upon the PCT application by the appropriate deadlines. Any patents that may issue from these applications are expected to expire no earlier than 2036, subject to any disclaimers or extensions.

TRV734

TRV734 is a small molecule μ-GPS that we discovered and have developed through Phase 1 as a first-line, orally administered compound for the treatment of moderate-to-severe acute and chronic pain. Like OLINVO, TRV734 takes advantage of a well-established mechanism of pain relief by targeting the μ-opioid receptor, but does so with enhanced selectivity for the G protein signaling pathway, which in preclinical studies was linked to analgesia, as opposed to the β-arrestin signaling pathway, which in preclinical studies was associated with side effects. Subject to successful preclinical and clinical development and regulatory approval, we believe TRV734 may have an improved efficacy and side effect profile as compared to current commonly prescribed oral analgesics, such as oxycodone. We intend to continue to focus our efforts for TRV734 on securing a worldwide development and commercialization partner for this asset.

TRV734 has shown a similar profile to OLINVO in in vitro and in vivo studies. It is highly selective for the μ-opioid receptor where, like the most powerful opioid analgesics, it is a strong agonist of G protein coupling. TRV734 is distinct from those analgesics in its very weak recruitment of β-arrestins to the μ-opioid receptor. In our preclinical studies, TRV734 showed analgesic effects in preclinical pain models similar to oxycodone and morphine. In the same studies, TRV734 caused less constipation compared to equivalently analgesic doses of oxycodone and morphine. TRV734 is active after oral administration in mice and rats, has high oral bioavailability and has been well tolerated in non-human primates.

We have completed three Phase 1 trials of TRV734 in healthy volunteers, including a single ascending dose study, a multiple ascending dose study, and a pharmacokinetic study. In these studies, a total of 127 healthy volunteers were exposed to TRV734 at doses between 2 mg and 250 mg. We incorporated measures to assess the potential for analgesic efficacy and tolerability advantages in these studies. Based on these data and data for OLINVO, we believe that TRV734 may offer an improved efficacy profile as compared to current opioid therapies or equivalent efficacy with an improved gastrointestinal tolerability and respiratory safety profile.

Our TRV734 patent portfolio is wholly owned by us and includes one issued U.S. patent (U.S. Patent No, 9,044,469) claiming TRV734, other compounds and/or methods of making or using the same. This patent is expected to expire no earlier than 2032, subject to any disclaimers or extensions. We also have issued patents in Japan and New Zealand claiming TRV734, other compounds and/or methods of making or using the same. The foreign portfolio also includes applications that have been allowed in China, Australia, and by the European Patent Office claiming TRV734, other compounds and/or methods of making or using the same. We also have patent applications pending in South Korea, the European Patent Office, the Eurasian Patent Office, Australia, Brazil, Canada, Israel, India, Japan, China, Hong Kong and New Zealand. The issued patents and patents that could issue in the future from these allowed or pending applications outside the United States are expected to expire no earlier than 2032, subject to any disclaimers or extensions.

TRV027

TRV027 is a peptide β-arrestin biased ligand that targets the angiotensin II type 1 receptor (AT1R), inhibiting angiotensin II-mediated G protein signaling and activating β-arrestin signaling. For the past several years, we have been developing TRV027 for the treatment of AHF in combination with standard diuretic therapy.

The current approach to treating patients with AHF involves facilitating the excretion of accumulated fluid with loop diuretics like furosemide; improving hemodynamics by reducing preload and afterload blood pressure with vasodilators like nitroglycerin; and directly stimulating the heart to contract more forcefully with inotropes like dobutamine. None of these approaches has been shown to greatly improve patient outcomes in AHF, and each therapy has specific adverse effects that limit its clinical utility.

Clinical development experience

In May 2016, we announced that TRV027 did not meet either the primary or secondary endpoints of the Phase 2b (BLAST-AHF), randomized, double-blind, standard of care controlled clinical trial evaluating the safety and efficacy of TRV027 in 618 patients with AHF. The study compared TRV027 (1.0 mg/hr, 5.0 mg/hr and 25 mg/hr) plus standard heart failure therapy versus placebo plus standard therapy. The primary objective of this trial was to evaluate the effects of TRV027 on a composite of clinically important outcomes: mortality, worsening heart failure, hospital readmission rate, dyspnea, and length of hospital stay. In this study, TRV027 or placebo were initiated after presentation to the hospital and then continued to be administered for a minimum of 48 hours and a maximum of 96 hours. Pre-specified analyses to identify populations that may respond best to TRV027 included segmentation by ejection fraction, systolic blood pressure, plasma renin activity, and glomerular filtration rate. The study methodology was published in the *Journal of the American College of Cardiology – Heart Failure* in March 2015.

Although the BLAST-AHF trial did not meet its primary or secondary endpoints, in a post-hoc analysis of patients with systolic blood pressure in the upper two tertiles (top two thirds), there were statistically significant improvements in long-term mortality and morbidity for the lowest tested dose of 1mg/hr. These data, in conjunction with a finding of improved serum creatinine at day 30 for TRV027 1 mg/hr compared to placebo as well as published preclinical data, suggest a new hypothesis that TRV027 may improve longer term outcomes based on its unique biased ligand mechanism. This mechanism has been linked to cytoprotective and anti-apoptotic effects. We are seeking a partner to fund future clinical testing of this hypothesis.

In addition to the BLAST-AHF trial, we have completed three clinical trials of TRV027:

- A Phase 2a clinical trial in medically fragile subjects with advanced stable heart failure, low ejection fraction and a clinical indication for right-heart catheterization. Ejection fraction is a measure of the volume of blood pumped by the heart. Right-heart catheterization is a procedure that allows measurement of intracardiac and intravascular pressures on the side of the heart leading to the lungs.

- A Phase 1b clinical trial in subjects with moderate heart failure and concomitant renal dysfunction. Selecting a stable population allowed us to directly measure renal plasma flow, or RPF, and glomerular filtration rate, or GFR, two common measures used to evaluate renal safety.

- A Phase 1 clinical trial in healthy subjects to evaluate pharmacokinetics and tolerability prior to moving into chronic stable heart failure subjects.

Option and License Agreements with Allergan

On May 3, 2013, we entered into an option agreement and a license agreement with Allergan plc (formerly Actavis plc and Forest Laboratories Holdings Limited), under which we granted to Allergan an exclusive option to license TRV027. In March 2015, we signed a letter agreement with Allergan pursuant to which Allergan paid us $10.0 million to fund the expansion of the Phase 2b trial of TRV027 in AHF from 500 patients to 620 patients. In August 2016, Allergan notified us of its decision to not exercise its exclusive option. As such, we have retained all rights to TRV027.

Intellectual Property

Our TRV027 patent portfolio is wholly owned by us. The portfolio includes four issued U.S. patents (U.S. Patent Nos. 8,486,885; 8,796,204; 8,809,260; and 8,993,511) that claim, among other things, TRV027, compositions comprising TRV027, and methods of using TRV027. We also have issued patents in Europe, Australia, Japan, New Zealand China, and Hong Kong. The issued U.S. patents covering the composition of matter and methods of using TRV027 are expected to expire no earlier than 2031 (U.S. Patent No. 8,486,885) and 2029 (U.S. Patent Nos. 8,796,204; 8,809,260; and 8,993,511), subject to any disclaimers or extensions available under the Hatch-Waxman Act. The issued European Patent is expected to provide coverage for TRV027 throughout most of European Union until at least 2029, subject to any disclaimers or extensions. The TRV027 patent portfolio also includes two pending U.S. patent applications, which claim a genus of compounds that would encompass TRV027 and methods of using such compounds. If the two pending U.S. patent applications were to issue, they would be expected to expire no earlier than 2029, subject to any disclaimers or extensions. Outside of the United States, we have pending patent applications in Canada and India that are directed to TRV027. The patents from these applications, if issued, are predicted to expire in 2029, subject to any disclaimers or extensions.

Additionally, the TRV027 patent portfolio includes one issued patent (U.S. Patent No. 9,518,086) directed to a crystalline form of TRV027, two U.S. non-provisional directed to, among other things, synthesis of TRV027, crystalline and amorphous forms of TRV027, and methods of preparing crystalline and amorphous forms of TRV027. We have foreign application directed to, among other things, crystalline and amorphous forms of TRV027, that are pending in Australia, Canada, China, Europe, Japan, and New Zealand. We also have foreign application directed to, among other things, synthesis of TRV027, that are pending in Australia, Canada, China, Europe, India, Japan, and New Zealand. U.S. Patent No. 9,518,086 covering a crystalline form of TRV027 is expected to expire no earlier than 2035, subject to any disclaimers or extensions. Any patents resulting from the pending patent applications, if issued are also expected to expire no earlier than 2035.

Our Platform

G protein coupled receptors, or GPCRs, are a large family of cell surface receptors that trigger two signaling pathways, G protein and β-arrestin, and are implicated in cellular function and disease processes. More than 30% of all currently marketed therapeutics target GPCRs. Currently available therapeutics that target GPCRs, or GPCR ligands, are typically not signal specific, and therefore either inhibit both the G protein and β-arrestin pathways (an antagonist ligand) or activate both pathways (an agonist ligand). This lack of signal specificity often results in a suboptimal therapeutic profile for these drugs because in many cases one of the pathways is associated with a beneficial therapeutic effect and the other is associated with limiting that benefit or with an undesirable side effect. We use our proprietary Advanced Biased Ligand Explorer, or ABLE, product platform to identify “biased” ligands, which are compounds that activate one of the two signaling pathways of the GPCR while inhibiting the other. This signaling specificity is the basis for our drug discovery and development approach, which is to identify selective GPCR biased ligands and develop them into differentiated clinical products. While some GPCRs trigger other signaling pathways in addition to G protein and β-arrestin, most GPCRs trigger those two pathways.

Our ABLE product platform is a collection of proprietary biological information, *in vitro* assays, know-how and expertise that we use to identify unique GPCR-targeted biased ligands with attractive pharmaceutical properties. *In vitro* assays are laboratory tests performed outside of a living organism. Our *in vitro* assays use cells that have the receptor of interest on the cell surface, where G protein and β-arrestin signaling from that receptor can be measured to determine if a particular ligand is biased, and if so whether it is a G protein or β-arrestin biased ligand. Our assays can also measure different cellular responses resulting from signaling through β -arrestin and can thereby help us to associate pharmacological responses with molecular signaling. Most components of our ABLE product platform are maintained as trade secrets, but the output of the product platform is reflected in the product candidates that we have advanced into clinical testing and the research we have published in numerous peer-reviewed journals. We believe that our ABLE product platform provides us with an important competitive advantage in identifying further opportunities for efficient and high-impact biased ligand drug discovery, development and commercialization.

We were founded in late 2007 to discover and develop product candidates based on biased ligands, a concept discovered by our scientific founder, Dr. Robert Lefkowitz, who was awarded the 2012 Nobel Prize in Chemistry in part for his elucidation of the multiple pathways that a GPCR engages. We believe that we are the first company to progress a GPCR biased ligand into clinical trials. The members of our executive management team have held senior positions at leading pharmaceutical and biotechnology companies and possess substantial experience across the spectrum of drug discovery, development, and commercialization.

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our product candidates, their methods of use, related technology and other inventions that are important to our business. We also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, maintain our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable patents and other proprietary rights of third parties. We also rely on know-how, and continuing technological innovation to develop, strengthen and maintain our proprietary position in the field of modulating GCPRs with biased ligands.

One or more third parties may hold intellectual property, including patent rights, that is important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially. If we were not able to obtain a license, or were not able to obtain a license on commercially reasonable terms, our business could be harmed, possibly materially.

We plan to continue to expand our intellectual property estate by filing patent applications directed to dosage forms, methods of treatment and additional biased modulators of GCPRs. We anticipate seeking patent protection in the United States and internationally for compositions of matter covering the compounds, the chemistries and processes for manufacturing these compounds and the use of these compounds in a variety of therapies.

The patent positions of biopharmaceutical companies like us 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 the patent's scope can be modified after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

Because many patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags behind actual

discoveries, we cannot be certain that we will be able to obtain patent protection for the inventions disclosed and/or claimed in our pending patent applications. Moreover, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office or a foreign patent office to determine priority of invention or in post-grant challenge proceedings, such as oppositions, *inter-partes* review, post grant review or a derivation proceeding, that challenge our entitlement to an invention or the patentability of one or more claims in our patent applications or issued patents. Such proceedings could result in substantial cost, even if the eventual outcome is favorable to us.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a PCT application or a non-provisional patent application, subject to any disclaimers or extensions. The term of a patent in the United States can be adjusted and extended due to the failure of the United States Patent and Trademark Office following certain statutory and regulation deadlines for issuing a patent.

In the United States, the patent term of a patent that covers an FDA-approved drug also may be eligible for patent term extension, which permits patent term restoration as compensation for a portion of the patent term lost during clinical development and the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under clinical development and regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other non-United States jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. Although, we intend to seek patent term extensions to any of our issued patents in any jurisdiction where these are available there is no guarantee that the applicable authorities, including the United States Patent and Trademark Office, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property.

Manufacturing

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if our product candidates receive marketing approval. At this time, none of our contract manufacturing agreements limit where, or with whom we can contract for commercial manufacture or distribution.

Commercialization

We have not yet fully established sales, marketing or product distribution infrastructure. Subject to successfully completing product development and receiving marketing approvals, we expect to commence commercialization activities for our wholly owned products by building a sales organization in the United States, initially in the hospital market. We believe that such an organization will be able to address the community of physicians who are the key specialists in treating the patient populations for which our product candidates are being developed. Outside the United States, we expect to enter into distribution and other commercial arrangements with third parties for any of our product candidates that obtain marketing approval. We also intend to license out commercial rights for products that require a substantial primary care presence.

In parallel with building our commercial organization, we plan to develop educational initiatives with respect to approved products and relationships with thought leaders in relevant fields of medicine.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Products in development by other companies may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain marketing approval.

Some of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early stage companies also may prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

The key competitive factors affecting the success of all of our therapeutic product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the level of generic competition and the availability of reimbursement from government and other third party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third party payors seeking to encourage the use of generic products. Generic products that broadly address these indications are currently on the market for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

FDA Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending new drug applications, or NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or

partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of human clinical trials, including adequate and well-controlled clinical trials, in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA;
- completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity, as well as satisfactory completion of an FDA inspection of selected clinical sites to determine GCP compliance;
- FDA review and approval of an NDA; and
- in certain cases, DEA review and scheduling activities prior to launch.

Preclinical Studies

Preclinical studies include laboratory evaluation of drug substance chemistry, toxicity and drug product formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Manufacture of drug substance, drug product and the labeling and distribution of clinical supplies must all comply with cGMP standards. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must continue to oversee the clinical trial while it is being conducted. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined. In Phase 1, the drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an initial indication of its effectiveness. In Phase 2, the drug typically is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. In Phase 3, the drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

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

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has agreed to certain performance goals regarding the timing of its review of an application.

In addition, under the Pediatric Research Equity Act an NDA or supplement to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, to mitigate any identified or suspected serious risks and ensure safe use of the drug. The REMS plan could include medication guides, physician communication plans, assessment plans and elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools. We expect that the μ-opioid agonist products will be subject to a REMS, since currently marketed opioid products are subject to this requirement.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA typically refers a question regarding a novel drug to an external advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured, referred to as a Pre-Approval Inspection, or PAI. The FDA will not approve an application unless it

determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCP.

The testing and approval process for an NDA requires substantial time, effort and financial resources, and each may take several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval of an NDA on a timely basis, or at all.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. For some products, an additional step of DEA review and scheduling is required.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, including a boxed warning, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization or impose other conditions, including distribution restrictions or other risk management mechanisms under a REMS which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Expedited Review and Approval

The FDA has various programs, including Fast Track, Breakthrough Therapy designation, priority review, and accelerated approval, that are intended to expedite or simplify the process for reviewing drugs, and/or provide for the approval of a drug on the basis of a surrogate endpoint. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will be shortened. Generally, drugs that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious or life-threatening diseases or conditions and fill unmet medical needs. In December 2015, FDA granted Fast Track designation to OLINVO for the management of moderate-to-severe acute pain. Priority review is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within six months as compared to a standard review time of ten months.

Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval, which is described in Subpart H of 21 Code of Federal Regulations, or 21 CFR Part 314, provides for an earlier approval for a new drug that is intended to treat a serious or life-threatening disease or condition and that fills an unmet medical need based on a surrogate endpoint. A surrogate endpoint is a clinical measurement or other biomarker used as an indirect or substitute measurement to predict a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a product candidate receiving accelerated approval perform post-marketing clinical trials.

In the Food and Drug Administration Safety and Innovation Act, which was signed into law in July 2012, Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of products under accelerated approval. The law required the FDA to issue related draft guidance within a year after the law's enactment and also promulgate confirming regulatory changes. In June 2013, the FDA published a draft Guidance for Industry entitled, "Expedited Programs for Serious Conditions—Drugs and Biologics" which provides guidance on FDA

programs that are intended to facilitate and expedite development and review of new drugs as well as threshold criteria generally applicable to concluding that a drug is a candidate for these expedited development and review programs. In addition to the Fast Track, accelerated approval and priority review programs discussed above, the FDA also provided guidance on a new program for Breakthrough Therapy designation. A Breakthrough Therapy designation is intended to expedite the development and FDA review of drugs for serious or life-threatening conditions or where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies. A request for Breakthrough Therapy designation should be submitted concurrently with, or as an amendment to an IND. In February 2016, OLINVO received a Breakthrough Therapy designation from the FDA for the management of moderate-to-severe acute pain in patients 18 years of age or older for whom a parenteral opioid is warranted.

Post-Approval Requirements

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

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

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Although physicians, in the practice of medicine, may prescribe approved drugs for unapproved indications,

pharmaceutical companies generally are required to promote their drug products only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

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

DEA Regulation

Both OLINVO and TRV734, if approved, will be regulated as a "controlled substance" as defined in the Controlled Substances Act of 1970, or CSA, which establishes registration, security, recordkeeping, reporting, storage, distribution and other requirements administered by the DEA. The DEA is concerned with the control of handlers of controlled substances, and with the equipment and raw materials used in their manufacture and packaging, in order to prevent loss and diversion into illicit channels of commerce.

The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use, and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. OLINVO and TRV734, if approved, are expected to be listed by the DEA as Schedule II controlled substances under the CSA. Consequently, their manufacture, shipment, storage, sale and use will be subject to a high degree of regulation.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized.

The DEA typically inspects a facility to review its security measures prior to issuing a registration. Security requirements vary by controlled substance schedule, with the most stringent requirements applying to Schedule I and Schedule II substances. Required security measures include background checks on employees and physical control of inventory through measures such as cages, surveillance cameras and inventory reconciliations. Records must be maintained for the handling of all controlled substances, and periodic reports made to the DEA, for example distribution reports for Schedule I and II controlled substances, Schedule III substances that are narcotics, and other designated substances. Reports must also be made for thefts or losses of any controlled substance, and to obtain authorization to destroy any controlled substance. In addition, special authorization and notification requirements apply to imports and exports.

In addition, a DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. Distributions of any Schedule I or II controlled substance must also be accompanied by special order forms, with copies provided to the DEA. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments. Our, or our contract manufacturers', quota of an active ingredient may not be sufficient to meet commercial demand or complete clinical trials. Any delay or refusal by the DEA in establishing our, or our contract manufacturers', quota for controlled substances could delay or stop our clinical trials or product launches.

To meet its responsibilities, the DEA conducts periodic inspections of registered establishments that handle controlled substances. Individual states also regulate controlled substances, and we and our contract manufacturers will be subject to state regulation with respect to the distribution of these products.

Federal and State Fraud and Abuse and Data Privacy and Security Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state fraud and abuse laws restrict business practices in the biopharmaceutical industry. These laws include anti-kickback and false claims laws and regulations as well as data privacy and security laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

The reach of the Anti-Kickback Statute was also broadened by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively PPACA, which, among other things, amended the intent requirement of the federal Anti-Kickback Statute such 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. In addition, PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. PPACA also created new federal requirements for reporting, by applicable manufacturers of covered drugs of payments and other transfers of value to physicians and teaching hospitals.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-reimbursable, uses.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with

pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, 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 federal or state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion from participation in government healthcare programs, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Coverage and Reimbursement

The commercial success of our product candidates and our ability to commercialize any approved product candidates successfully will depend in part on the extent to which governmental payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers and other third party payors provide coverage for and establish adequate reimbursement levels for our product candidates. Government health administration authorities, private health insurers and other organizations generally decide which drugs they will pay for and establish reimbursement levels for healthcare. In particular, in the United States, private health insurers and other third party payors often provide reimbursement for products and services based on the level at which the government provides reimbursement through the Medicare or Medicaid programs for such treatments. In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and third party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which often has resulted in average selling prices lower than they would otherwise be. Further, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical coverage and reimbursement policies and pricing in general.

Third party payors are increasingly imposing additional requirements and restrictions on coverage and limiting reimbursement levels for medical products. For example, federal and state governments reimburse covered prescription drugs at varying rates generally below average wholesale price. These restrictions and limitations influence the purchase of healthcare services and products. Third- party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication. Third party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development. Legislative proposals to reform healthcare or reduce costs under government insurance programs may result in lower reimbursement for our products and product candidates or exclusion of our products and product candidates from coverage. The cost containment measures that healthcare payors and providers are instituting and any healthcare reform could significantly reduce our revenue from the sale of any approved product candidates. We cannot provide any assurances that we will be able to obtain and maintain third party coverage or adequate reimbursement for our product candidates in whole or in part.

Impact of Healthcare Reform on Coverage, Reimbursement and Pricing

The United States and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant

interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Part D plans include both standalone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for any products for which we receive marketing approval. However, any negotiated prices for our future products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from Medicare Part D may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes of Health, and periodic reports on the status of the research and related expenditures will be made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. If third party payors do not consider our product candidates to be cost-effective compared to other available therapies, they may not cover our product candidates, once approved, as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

PPACA became law in March 2010 and substantially changes the way healthcare is financed by both governmental and private insurers. Among other cost containment measures, the PPACA establishes an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; a new Medicare Part D coverage gap discount program; and a new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program. In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we are able to charge for our product candidates, once approved, or the amounts of reimbursement available for our product candidates once they are approved.

In addition, other legislative changes have been proposed and adopted since PPACA was enacted. In August 2011, the Budget Control Act of 2011, as amended, was signed into law. Among other things, this law created the Joint Select Committee on Deficit Reduction to propose spending reductions to Congress. The Joint Select Committee on Deficit Reduction did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions include aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 became law, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These and other healthcare reform initiatives may result in additional reductions in Medicare and other healthcare funding. In 2017, President Trump and the Republican Congressional leadership have vowed to repeal and replace PPACA. We cannot anticipate what impact any such replacement or other future healthcare reform initiatives will have on coverage and reimbursement of our products or our business more generally.

Exclusivity and Approval of Competing Products

Hatch-Waxman Patent Exclusivity

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA, or 505(b)(2) NDA. Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths, dosage form and route of administration as the listed drug and has been shown to be bioequivalent through *in vitro* or *in vivo* testing or otherwise to the listed drug. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug. 505(b)(2) NDAs generally are submitted for changes to a previously approved drug product, such as a new dosage form or indication.

The ANDA or 505(b)(2) NDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. Specifically, the applicant must certify with respect to each patent that:

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

Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except when the ANDA or 505(b)(2) NDA applicant challenges a listed drug. A certification that the proposed product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA or 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of notice of the Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

Hatch-Waxman Non-Patent Exclusivity

Market and data exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the activity of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or noninfringement.

The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant, are deemed by the FDA to be essential to the approval of the application or supplement. Three-year exclusivity may be awarded for changes to a previously approved drug product, such as new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent exclusivity periods described above. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or Orange Book listed patent protection cover the drug are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve an ANDA or 505(b)(2) application owing to regulatory exclusivity or listed patents. When any of our products is approved, we anticipate seeking pediatric exclusivity when it is appropriate.

Foreign Regulation

To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. For example, in the European Union, we must obtain authorization of a clinical trial application, or CTA, in each member state in which we intend to conduct a clinical trial. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Employees

As of December 31, 2016, we had 72 employees, all of whom are located in the United States. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate Information

We were incorporated under the laws of the State of Delaware in November 2007. Our principal executive offices are located at 1018 West 8th Avenue, Suite A, King of Prussia, Pennsylvania 19406. Our telephone number is (610) 354-8840.

Available Information

Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and other filings with the United States Securities and Exchange Commission, or the SEC, and all amendments to these filings, are available, free of charge, on our website at www.trevenainc.com as soon as reasonably practicable following our filing of any of these reports with the SEC. You can also obtain copies free of charge by contacting our Investor Relations

department at our office address listed below. The public may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street NE, Room 1580, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy, and information statements, and other information regarding issuers that file electronically with the SEC at www.sec.gov. The information posted on or accessible through these websites are not incorporated into this filing.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our initial public offering in February 2014, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeded $700.0 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. We refer to the Jumpstart Our Business Startups Act of 2012 in this Annual Report on Form 10-K as the "JOBS Act," and references to "emerging growth company" have the meaning associated with it in the JOBS Act.

EXECUTIVE OFFICERS OF THE REGISTRANT

Name	Age	Position
Maxine Gowen, Ph.D.	58	President, Chief Executive Officer and Director
Carrie L. Bourdow	54	Senior Vice President and Chief Commercial Officer
Roberto Cuca	49	Senior Vice President and Chief Financial Officer
Yacoub Habib, Ph.D.	49	Senior Vice President, Business Development and Corporate Planning
Michael W. Lark, Ph.D.	59	Senior Vice President, Research and Chief Scientific Officer
John M. Limongelli, Esq.	47	Senior Vice President, General Counsel and Chief Administrative Officer
David Soergel, M.D.	49	Senior Vice President, Clinical Development and Chief Medical Officer

Maxine Gowen, Ph.D.

Dr. Gowen has served as our President and Chief Executive Officer and as a member of our board of directors since our founding in November 2007. Prior to joining our company, Dr. Gowen was Senior Vice President for the Center of Excellence for External Drug Discovery at GlaxoSmithKline plc, or GSK, where she held a variety of leadership positions during her tenure of 15 years. Before GSK, Dr. Gowen was Senior Lecturer and Head, Bone Cell Biology Group, Department of Bone and Joint Medicine, of the University of Bath, U.K. Dr. Gowen has served as a director of Akebia Therapeutics, Inc. since July 2014 and Idera Pharmaceuticals, Inc. since January 2016. From 2008 until 2012, Dr. Gowen served as a director of Human Genome Sciences, Inc., a public biopharmaceutical company. Dr. Gowen also serves on the boards of BIO, the biotechnology industry association, and its affiliate, Life Sciences PA. She received her Ph.D. from the University of Sheffield, U.K., an M.B.A. with academic honors from The Wharton School of the University of Pennsylvania, and a B.Sc. with Honors in Biochemistry from the University of Bristol, U.K.

Carrie L. Bourdow

Ms. Bourdow has served as our Senior Vice President and Chief Commercial Officer since May 2015. From May 2013 to May 2015, she was Vice President of Marketing at Cubist Pharmaceuticals, Inc. Prior to joining Cubist in 2013, Ms. Bourdow served for more than 20 years at Merck & Co., Inc., where she held positions of increasing responsibility across several therapeutic areas including anti-infectives, acute heart failure, and pain. Ms. Bourdow earned her B.A. from Hendrix College and her M.B.A. from Southern Illinois University.

Roberto Cuca

Mr. Cuca joined our company as Senior Vice President and Chief Financial Officer in September 2013. Prior to joining us, he held various leadership positions in the finance organization of Endo Health Solutions Inc., a pharmaceutical company, from March 2010 to August 2013, including, most recently, Treasurer and Senior Vice President, Finance. Prior to that, he was Director, Corporate and Business Development, at moksha8 Pharmaceuticals, Inc., an emerging markets-focused pharmaceutical company, from March 2008 until February 2010. From 2005 until 2008, he worked at JPMorgan Chase & Co. as an equity analyst covering U.S. pharmaceutical

companies. Mr. Cuca received an M.B.A. from the Wharton School of The University of Pennsylvania, a J.D. from Cornell Law School, an A.B. from Princeton University, and he is a CFA charterholder.

Yacoub Habib, Ph.D.

Dr. Habib has served as our Senior Vice President, Business Development and Corporate Planning since July 2015. Previously, from 2009 to June 2015, he served as Vice President of Business Development at Ikaria, Inc. and led the business development strategy for the company until its acquisition. From 2007 to 2009, he served as Executive Director of New Business Development for Pfizer Inc. Before joining Pfizer, Dr. Habib was Executive Director of Global Business Development for Organon Pharmaceuticals, a division of Akzo Nobel, where he was responsible for the identification, evaluation, and negotiation of in-licensing, out-licensing and divestiture opportunities in neuroscience, fertility, and women health. He started his career at Bristol-Myers Squibb where he spent nine years in various research, corporate, and business development roles including as Director of Corporate and Business Development. Dr. Habib holds a Ph.D. in pharmaceutical sciences from the University of Maryland and an M.B.A. with a major in finance and marketing from New York University Stern School of Business.

Michael W. Lark, Ph.D.

Dr. Lark has served in a number of capacities with our company since February 2008, and since March 2011 has served as Senior Vice President, Research and Chief Scientific Officer. Prior to joining our company, he was Vice President of Biology at Centocor Inc., a division of Johnson & Johnson, or Centocor, from 2004 until 2008 and the Senior Director of Cardiovascular and Metabolic Diseases at Centocor from 2002 to 2004. Prior to that, Dr. Lark was Director of Musculoskeletal Diseases at GSK, from 1999 until 2002. Dr. Lark received his Ph.D. in Molecular Biology and Microbiology from the Case Western Reserve University Medical School and his B.S. in Microbiology from the Pennsylvania State University.

John M. Limongelli, Esq.

Mr. Limongelli joined our company as Senior Vice President, General Counsel and Corporate Secretary in May 2014 and was appointed Chief Administrative Officer in March 2016. Prior to this, he was Vice President, Associate Chief Counsel and Corporate Secretary at Cigna Corporation from September 2013 until May 2014. From October 2012 to September 2013, he was a partner at the law firm Royer Cooper Cohen Braunfeld LLC. He served as Senior Vice President, General Counsel and Secretary at Adolor Corporation from September 2008 until December 2011. Prior to Adolor, Mr. Limongelli held roles of increasing responsibility with Cephalon, Inc., most recently serving as Vice President and Associate General Counsel. Mr. Limongelli began his legal career in private practice with Morgan, Lewis & Bockius, LLP. Prior to his legal career, Mr. Limongelli was a certified public accountant with KPMG LLP. Mr. Limongelli obtained both his J.D. and M.B.A. from Temple University.

David Soergel, M.D.

Dr. Soergel has served in multiple positions since joining our company in November 2009 and currently serves as our Senior Vice President, Clinical Development and Chief Medical Officer. Prior to joining our company, he served as Senior Director, Clinical Development for Concert Pharmaceuticals, Inc., a biotechnology company, from July 2008 to November 2009. Prior to Concert, Dr. Soergel served as Director, Discovery Medicine, in the Cardiovascular Urogenital Center of Excellence in Drug Discovery at GSK, from 2005 until 2008. Dr. Soergel received an M.D. from Cornell University Medical College and a B.A. from The Johns Hopkins University. Dr. Soergel completed his clinical training in pediatric cardiology at Johns Hopkins Hospital and underwent additional training in heart failure and transplant at the Children's Hospital of Philadelphia.

ITEM 1A. RISK FACTORS

Our business is subject to numerous risks. You should carefully consider the following risks and all other information contained in this Annual Report on Form 10-K, as well as general economic and business risks, together with any other documents we file with the SEC. If any of the following events actually occur or risks actually materialize, it could have a material adverse effect on our business, operating results and financial condition and cause the trading price of our common stock to decline.

Risks Related to Our Financial Position and Capital Needs

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $103.0 million, $50.5 million and $49.7 million for the years ended December 31, 2016, 2015, and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of $285.6 million. To date, we have financed our operations primarily through private placements and public offerings of our equity securities and debt borrowings. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials. We still have not completed development of any of our product candidates. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- complete enrollment in the remaining Phase 3 clinical trial of OLINVO, our lead product candidate;
- establish sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize OLINVO and any other products that we choose not to license to a third party and for which we may obtain regulatory approval;
- initiate clinical trials for TRV250, our δ-opioid receptor product candidate;
- seek to discover additional product candidates;
- conduct clinical trials and seek regulatory approvals for any product candidates that successfully complete clinical trials;
- maintain, expand, and protect our intellectual property portfolio;
- hire additional clinical and scientific personnel; and
- add operational, financial, and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, potentially entering into collaboration and license agreements, obtaining regulatory approval for product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of some of these activities and have not begun others. We may never succeed in these activities and, even if we do, may never achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product 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 FDA or foreign regulatory authorities, to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials, making necessary regulatory filings, or the development of any of our product candidates, our expenses could increase.

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

We will need substantial additional funding, which may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we complete enrollment in the remaining Phase 3 clinical trial for OLINVO, continue research and development, and initiate additional clinical trials of, and seek regulatory approval for, OLINVO and our other product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales, and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to:

- delay, reduce, or eliminate our research and development programs or any future commercialization efforts;
- relinquish or license on unfavorable terms our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves;
- seek collaborators for one or more of our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or
- cease operations altogether.

We estimate that our existing cash and cash equivalents and marketable securities as of December 31, 2016, together with interest thereon, will enable us to fund our operating expenses and capital expenditure requirements into the second quarter of 2018. Accordingly, we expect that we will need to raise substantial additional funds in the future. Our future capital requirements will depend on many factors, including:

- the progress and results of the Phase 3 clinical program for OLINVO;
- the scope, progress, results and costs of preclinical development, laboratory testing, and clinical trials for our other product candidates, including TRV250;
- our ability to enter into collaborative agreements for the development and commercialization of our product candidates, including OLINVO in regions outside the United States;
- the number and development requirements of other product candidates that we pursue;
- the costs, timing and outcome of regulatory review of our product candidates or any future product candidates, both in the United States and in territories outside the United States;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales, and distribution, for any of our product candidates for which we receive marketing approval;
- any product liability or other lawsuits related to our products;
- the expenses needed to attract and retain skilled personnel;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; and
- the costs involved in preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights, and defending any intellectual property-related claims, both in the United States and in territories outside the United States.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete. Despite these efforts, we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. For example, in May 2016, we announced that TRV027 failed to meet either the primary or secondary endpoints of the BLAST-AHF Phase 2b clinical trial. In addition, our product candidates, if approved, may not achieve commercial success or meet our expectations. Our commercial revenue, if any, will be derived from sales of products that we do not expect to be commercially available for at least two 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. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

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

Until such time, if ever, as we can generate substantial product revenue and positive cash flows from operations, we expect to finance our cash needs through a combination of equity offerings, debt financings, and license and development agreements in connection with any collaborations. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, either at the time of such capital raise or thereafter, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Preferred equity financing and additional 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 additional funds through collaborations, strategic alliances, or marketing, distribution 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 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.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced active operations in late 2007, and our activities to date have been limited to, among other things, organizing and staffing our company, business planning, raising capital, developing our ABLE product platform, identifying potential product candidates, undertaking preclinical studies and conducting clinical trials. With the exception of OLINOVO, our product candidates are early in development. We have not yet demonstrated our ability to successfully complete all necessary later stage clinical trials, obtain regulatory approvals, manufacture a product at commercial scale or arrange for a third party to do so on our behalf, or conduct sales, marketing, and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as reliable as they could be if we had a longer operating history.

In addition, as a young business, we may encounter unforeseen expenses, difficulties, complications, delays, and other known and unknown factors. We will need to significantly expand our capabilities to support future activities related to the approval, manufacture, and commercialization of our product candidates. We may be unsuccessful in adding such capabilities.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any past quarterly or annual periods as indications of future operating performance.

Risks Related to the Discovery and Development of Our Product Candidates

Our research and development efforts are focused on discovering and developing novel drugs based on biased ligands, and the approach we are taking to discover and develop drugs is not proven and may never lead to marketable products.

The discovery and development of drugs based on biased ligands is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop product candidates are relatively new. The scientific evidence to support the feasibility of developing differentiated product candidates based on these discoveries is both preliminary and limited. We believe that we are the first company to conduct a clinical trial of a product candidate based on the concept of biased ligands. Therefore, we do not know if our approach will be successful or will ultimately lead to the approval of any current or future product candidate.

We are early in our development efforts and have only one product candidate, OLINVO, in Phase 3 development. If we are unable to successfully complete development and commercialization of our product candidates, either on our own or with a partner, or experience significant delays in doing so, our business will be materially harmed.

We are early in our development efforts and have only one product candidate, OLINVO, that is in Phase 3 development. We have invested substantially all of our efforts and financial resources in the identification and development of biased ligands. Our ability to generate product revenue, which we do not expect will occur for at least two years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining, maintaining, and protecting our intellectual property portfolio, including patents and trade secrets, and regulatory exclusivity for our product candidates;
- making arrangements with third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community, and third party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage of our products and adequate reimbursement; and
- maintaining a continued acceptable safety profile of our products following approval.

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

Even though OLINVO has received breakthrough therapy designation and fast track designation for the management of moderate-to-severe acute pain, there can be no assurance that such designations will result in expedited review or approval.

Breakthrough therapy designation and fast track designation are intended to expedite the development and review of products that address unmet medical needs for serious conditions. We have received breakthrough therapy designation and fast track designation for OLINVO for the management of moderate-to-severe acute pain, but there can be no assurance that such designations ultimately will result in expedited review or approval. Furthermore, the FDA may

rescind the breakthrough therapy designation if it determines that subsequent data no longer support the designation. Fast track designation and breakthrough therapy designation do not change the standards for product approval.

The reported results of OLINVO are based on top-line data and may ultimately differ from actual results once additional data are received and fully evaluated.

The reported results of OLINVO that we have publicly disclosed, and that are discussed herein, consist of top-line data. Top-line data are based on a preliminary analysis of currently-available efficacy and safety data, and therefore the reported results, findings and conclusions related to OLINVO are subject to change following a comprehensive review of the more extensive data that we expect to receive related to OLINVO. Top-line data are based on important assumptions, estimations, calculations, and information currently available to us, and we have not received or had an opportunity to fully and carefully evaluate all of the data related to OLINVO. As a result, the top-line results of OLINVO that we have reported may differ from future results, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. In addition, third parties, including regulatory agencies, may not accept or agree with our assumptions, estimations, calculations or analyses or may interpret or weigh the importance of data differently, which could impact the value of OLINVO, the approvability or commercialization of OLINVO, and our business in general. If the top-line data that we have reported related to OLINVO differ from actual results, our ability to obtain approval for, and commercialize, our products may be harmed, which could harm our business, financial condition, operating results or prospects.

We may not be successful in our efforts to expand our pipeline of product candidates.

One element of our strategy is to expand our pipeline of therapeutics based on biased ligands and advance these product candidates through clinical development for the treatment of a variety of indications. Although our research and development efforts to date have resulted in a number of development programs based on biased ligands, we may not be able to develop product candidates that are safe and effective. Even if we are successful in continuing to expand our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our technological approach, we will not be able to obtain product revenue in future periods, which would make it unlikely that we would ever achieve profitability.

Preclinical and clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Clinical testing is expensive, can take many years to complete, and has a high risk of failure. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data often are susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. We may experience numerous unforeseen events during, or as a result of, clinical trials, which could delay or prevent our ability to receive marketing approval or subsequently to commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at prospective trial sites;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;

- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

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

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications 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 and/or reporting requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs also will increase if we experience delays in testing or in receiving marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, thereby harming our business and results of operations.

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. Some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates, and patients who would otherwise be eligible for our

clinical trials may instead enroll in clinical trials of our competitors' product candidates. Patient enrollment is affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

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

If serious adverse or unacceptable side effects are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.

If our product candidates are associated with adverse side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk-benefit perspective. In our industry, many compounds that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the compound or significantly limited its commercial opportunity. In the event that our clinical trials reveal a high and unacceptable severity and prevalence of side effects, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development or deny approval of our product candidates for any or all targeted indications. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial and could result in potential product liability claims.

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

- regulatory authorities may require additional warnings on the label or even withdraw approvals of such product;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients, if one is not required in connection with regulatory approval;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved.

OLINVO is predominantly metabolized by two liver enzymes, CYP2D6 and CYP3A4, that are common metabolic pathways for drugs. Because of competitive use of these pathways, we may need to conduct additional drug

interaction studies and OLINVO may be limited in its co-administration with other drugs using these pathways as their safety and effectiveness, as well as OLINVO's, may be adversely affected. This could limit our commercial opportunity due to the common co-administration of drugs in patients with moderate-to-severe acute pain requiring IV therapy. In addition, since CYP2D6 enzyme activity varies in the population, different dosing may be required in the product label for individuals that have low levels of CYP2D6 activity, which could limit the commercial opportunity of the drug, if approved. We continue to discuss this question with the FDA and cannot assure you that the FDA will not require us to utilize different dosing for this population and/or prospectively characterize individuals' CYP2D6 activity prior to administering OLINVO.

OLINVO and TRV734 are both biased ligands targeted at the μ-opioid receptor. Common adverse reactions for agonists of the μ-opioid receptor include respiratory depression, constipation, nausea, vomiting, and addiction. In rare cases, μ-opioid receptor agonists can cause respiratory arrest requiring immediate medical intervention. Since OLINVO and TRV734 also modulate the μ-opioid receptor, these adverse reactions and risks likely will apply to the use of OLINVO and TRV734. One healthy subject in the 0.25 mg dosing cohort of our Phase 1 clinical trial of OLINVO experienced a severe episode of vasovagal syncope during which he fainted and his pulse stopped. These were considered severe adverse events. It is possible that serious adverse vasovagal events could occur in other patients dosed with OLINVO. Agonists at the Ω-opioid receptor have been associated with a risk of seizures. TRV250, our Ω-opioid receptor product candidate, targets the same receptor as other programs that have been associated with seizures and, accordingly, it is possible that it will be associated with similar side effects. In such case, we likely would discontinue further development of TRV250 for the treatment of migraines.

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

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have fewer clinical or regulatory risks and/or greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Risks Related to the Commercialization of Our Product Candidates

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

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors, and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy, safety and potential advantages compared to alternative treatments;
- the timing of market introduction of the product candidate as well as competitive products;
- our ability to offer the product for sale profitably and 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 sales, marketing, and distribution support;
- the availability of third party coverage and adequate reimbursement;
- the prevalence and severity of any side effects;
- the clinical indications for which the product is approved; and
- any restrictions on the use of our products, both on their own and together with other medications.

If we are unable to establish manufacturing, sales, marketing, and distribution capabilities or to enter into agreements with third parties to produce, market, and sell our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We currently have limited resources focused on the manufacturing, marketing, sales and distribution of pharmaceutical products and have limited experience and capabilities in this area. To commercialize any product candidates that receive marketing approval, we would need to build manufacturing, marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If we successfully develop and obtain regulatory approval for any of our product candidates, we expect to build a targeted specialist sales force to market or co-promote the product in the United States; we currently do not expect to build sales, manufacturing and distribution capabilities outside of the United States, although this expectation could change in the future. There are substantial risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

There are a number of factors that may inhibit our efforts to commercialize our products on our own, including:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary or other products to be offered by sales personnel, which may put us at a competitive disadvantage from the perspective of sales efficiency relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

As an alternative to establishing our own sales force, we may choose to partner with third parties that have well-established direct sales forces to sell, market and distribute our products, particularly in markets outside of the United States. If we are unable to enter into collaborations with third parties for the commercialization of approved products, if any, on acceptable terms or at all, or if any such partner does not devote sufficient resources to the commercialization of our product or otherwise fails in commercialization efforts, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval.

For OLINVO, we will need to partner with one or more third parties to sell, market and distribute this product, if approved, outside the United States. We may be unsuccessful in our efforts to secure such partnerships.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. In addition to existing therapeutic treatments for the indications we are targeting with our product candidates, which our goal would be to displace or to be used in conjunction with, if any of our product candidates achieves regulatory approval, we also face potential competition from other drug candidates in development by other companies. OLINVO also may compete against, or be used in combination with, OFIRMEV®, marketed by Mallinckrodt plc, EXPAREL®, marketed by Pacira Pharmaceuticals, Inc., CALDOLOR®, marketed by Cumberland Pharmaceuticals, DYLOJECT™, marketed by Pfizer Inc., and IONSYS® marketed by The Medicines Company. In addition to currently marketed IV analgesics, we are aware of a number of products in development that are aimed at improving the treatment of moderate-to-severe acute pain. AcelRx Pharmaceuticals, Inc. is developing a range of acute pain products involving sufentanil oral nanotabs in hand-held dispensers (DSUVIA™ and ZALVISO™). Durect Corporation, Innocoll Holdings plc, and Heron Therapeutics all have proprietary long-acting reformulations of bupivacaine in development. Recro Pharmaceuticals is developing an IV version of the NSAID meloxicam. Cara Therapeutics Inc. is developing an IV and oral peripherally restricted &-opioid receptor agonist, which has been administered in combination with μ-opioids in clinical trials. Some of these potential competitive compounds are being developed by large, well-financed, and experienced pharmaceutical and biotechnology companies, or have been partnered with such companies, which may give them development, regulatory and marketing advantages over us.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third party payors seeking to encourage the use of generic products. Generic products are currently on the market for the indications that we are pursuing. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competing generic products.

Some of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise than we do in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and selling and marketing approved products. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies also may prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Even if we or any future collaborators are able to commercialize any of our product candidates, the product candidates may become subject to unfavorable pricing regulations, third party coverage and reimbursement policies, healthcare reform initiatives, or regulatory or political concerns.

Both our and our collaborators' ability to commercialize any of our product candidates successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government payor programs at the federal and state level, including Medicare and Medicaid, private health insurers, managed care plans and other organizations. Government authorities and third party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. In addition, for hospital products, a private health insurer or Medicare will typically reimburse a fixed fee for certain procedures, including in-patient surgeries. Pharmaceutical products such as OLINVO, if approved, that may be used in connection with the surgery generally will not be separately reimbursed and, therefore, a hospital would have to assess the cost of OLINVO, if approved, relative to its benefits. Current or future efforts to limit the level of reimbursement for in-patient hospital procedures could cause a hospital to decide not to use OLINVO, if approved by the FDA. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular

medications or procedures. Increasingly, third party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any drug that we or our collaborators commercialize and, even if these are available, the level of reimbursement for a product or procedure may not be satisfactory. Inadequate reimbursement levels may adversely affect the demand for, or the price of, any product candidate for which we or our collaborators obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to seek to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we or our collaborators may not be able to successfully commercialize any product candidates for which marketing approval is obtained.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or analogous regulatory authorities outside the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution expenses. Interim reimbursement levels for new drugs, if applicable, also may not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our or our collaborators' inability to promptly obtain coverage and adequate reimbursement rates from both government- funded and private payors for any approved drugs that we develop could adversely affect our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drugs vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we or our collaborators might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay commercial launch of the drug, possibly for lengthy time periods, and negatively impact our ability to generate revenue from the sale of the drug in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

In addition to the above factors, the approval and commercialization of OLINVO may be negatively impacted by changing perceptions in the United States and elsewhere among regulators, legislators, and the general public concerning the approval, use, and abuse of prescription opioid products. In the future, the FDA and other regulatory and legislative bodies may enact regulations that seek to limit opioid prescribing and use. In response to these efforts and changing perceptions, physicians may determine to reduce the volume of opioid prescriptions they prescribe to patients. Any of these changes could negatively impact both the timing and likelihood of FDA approval of OLINVO, as well as the commercial opportunity, if approved.

There can be no assurance that our product candidates, if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication, that they will be considered cost-effective by third party payors, that coverage or an adequate level of reimbursement will be available, or that third party payors' reimbursement policies will not adversely affect our ability to profitably sell our product candidates if they are approved for sale.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical

testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- significant costs to defend the related litigation;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently maintain $15 million in product liability insurance coverage, which may be inadequate to cover all liabilities that we may incur. We will likely need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. 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.

Risks Related to Our Dependence on Third Parties

Any future relationships or collaborations we may enter into may be important to us. If we are unable to maintain our relationship with any of these collaborations, or if our relationship with these collaborators is not successful, our business could be adversely affected.

We have limited capabilities for product development, sales, marketing and distribution. For our product candidates, we may in the future determine to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of these candidates. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for collaboration 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 a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform and our business may be materially and adversely affected.

Any future collaborations we might enter into with another third party, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may elect not to continue development or commercialization programs or may not pursue commercialization of any product candidates that achieve regulatory approval based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could fail to make timely regulatory submissions for a product candidate;
- collaborators may not comply with all applicable regulatory requirements or may fail to report safety data in accordance with all applicable regulatory requirements;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to limit or eliminate efforts and resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated at the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If any collaborations we might enter into in the future do not result in the successful development and commercialization of products or if one of our 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, our development of our product platform and product candidates could be delayed and we may need additional resources to develop our product candidates and our product platform. The risks relating to our

product development, regulatory approval and commercialization described in this Annual Report also apply to the activities of our therapeutic program collaborators.

If a future collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our reputation in the business and financial communities could be adversely affected.

We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or complying with applicable regulatory requirements.

We rely on third party contract research organizations and clinical research organizations to conduct some of our preclinical studies and all of our clinical trials for our product candidates. We expect to continue to rely on third parties, such as contract research organizations, clinical research organizations, clinical data management organizations, medical institutions, and clinical investigators, to conduct some of our preclinical studies and all of our clinical trials. The agreements with these third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that could delay our product development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the general investigational plan and protocols for the trial and for ensuring that our preclinical studies are conducted in accordance with good laboratory practice, or GLP, as appropriate. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical investigators, and trial sites. If we or any of our clinical research organizations fail to comply with applicable GCPs, 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. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practice, or cGMP, regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

The third parties with whom we have contracted to help perform our preclinical studies or clinical trials also may have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

If any of our relationships with these third party contract research organizations or clinical research organizations terminate, we may not be able to enter into arrangements with alternative contract research organizations or clinical research organizations or to do so on commercially reasonable terms. Switching or adding additional contract research organizations or clinical research organizations involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new contract research organization or clinical research organization commences work. As a result, delays could occur that could compromise our ability to meet our desired development timelines. Although we seek to carefully manage our relationships with our contract research organizations and clinical research organizations, there can be no assurance that we will not encounter similar challenges or delays in the future.

We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We have limited internal manufacturing capabilities and do not have any manufacturing facilities. In addition, our product candidates have never been manufactured at commercial scale. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture, if any, of our product candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We also expect to rely on third party manufacturers or third party collaborators for the manufacture of commercial supply of any product candidates for which our collaborators or we obtain marketing approval. We may be unable to establish any agreements with third party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third party manufacturers, reliance on third party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- manufacturing delays if our third party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

The facilities used by our contract manufacturers to manufacture our product candidates and, potentially in the future, our products must be approved by the FDA pursuant to inspections that will be conducted after we submit an NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturers for compliance with current cGMP regulations for manufacture of our product candidates. Third party manufacturers may not be able to comply with the cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Our product candidates and any products that we may commercialize likely will compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. We may incur added costs and delays in identifying and qualifying any replacement manufacturers.

The U.S. Drug Enforcement Administration, or DEA, restricts the importation of a controlled substance finished drug product when the same substance is commercially available in the United States, which could reduce the number of potential alternative manufacturers for our μ-opioid receptor targeted product candidates, including OLINVO. In addition, a DEA quota system controls and limits the availability and production of controlled substances and the DEA also has authority to grant or deny requests for quota of controlled substances, which will likely include the active ingredients in OLINVO. Supply disruptions could result from delays in obtaining DEA approvals for controlled

substances or from the receipt of quota of controlled substances that are insufficient to meet future product demand. The quota system also may limit our ability to build inventory as a method for mitigating possible supply disruptions if OLINVO is approved for sale in the United States.

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

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

We rely on clinical data and results obtained by third parties that could ultimately prove to be inaccurate or unreliable.

As part of our strategy to mitigate development risk, we seek to develop product candidates with validated mechanisms of action and we utilize biomarkers to assess potential clinical efficacy early in the development process. This strategy necessarily relies upon clinical data and other results obtained by third parties that may ultimately prove to be inaccurate or unreliable. Further, such clinical data and results may be based on products or product candidates that are significantly different from our product candidates. If the third party data and results we rely upon prove to be inaccurate, unreliable or not applicable to our product candidates, we could make inaccurate assumptions and conclusions about our product candidates and our research and development efforts could be compromised.

Risks Related to Our Intellectual Property

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, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.

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 product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our 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. 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. Should we enter into collaborations with third parties, we may be required to consult with or cede control to collaborators regarding the prosecution, maintenance and enforcement of our patents. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of 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. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after a first filing, or in some cases 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 products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The Leahy-Smith America Invents Act, or the Leahy-Smith Act, 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 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 continues to develop and implement 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.

Moreover, we may be subject to a third party preissuance submission of prior art to the United States Patent and Trademark Office, 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, render unenforceable, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. 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.

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

The issuance of a patent does not foreclose challenges to its inventorship, scope, validity or enforceability. Therefore, 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 products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, rendered unenforceable, or interpreted narrowly.

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially.

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

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the United States Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are currently party to license agreements for technologies that we use in conducting our drug discovery activities. In the future, we may become party to licenses that are important for product development and commercialization. If we fail to comply with our obligations under current or future license and funding agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product or utilize any technology that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could materially and adversely affect the value of a product candidate being developed under any such agreement or could restrict our drug discovery activities. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

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

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

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

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

In addition to seeking patent protection for our product candidates, we rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We limit disclosure of such trade secrets where possible, but we also seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who do have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to timely commercialize, or to commercialize at all, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside the United States. Failure to obtain marketing approval for our product candidates will prevent us from commercializing these product candidates and will significantly limit our ability to generate revenue in the future. To date, we have not received approvals to market any of our product candidates from regulatory authorities in any jurisdiction and we may never be successful in obtaining any such approvals.

We have only limited experience in filing and supporting the applications necessary to gain marketing approvals, and we expect to rely on third parties to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. For OLINVO, if we submit an NDA, we expect the FDA to convene an Advisory Committee as part of the review process. The feedback received from an Advisory Committee can have a substantial impact on the FDA's decision to approve or reject a product candidate. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical studies or clinical trials. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval, the commercial prospects for our product candidates may be harmed and our ability to generate revenue may be materially impaired. Furthermore, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate or that includes language, such as a black box warning, that may impair our ability to successfully commercial that product candidate. Any of these scenarios could compromise the commercial prospects for our product candidates.

We anticipate that our μ-opioid receptor targeted product candidates, including OLINVO, will require Risk Evaluation and Mitigation Strategies, which could delay the approval of these product candidates and increase the cost, burden and liability associated with the commercialization of these product candidates.

The FDA Amendments Act of 2007 implemented safety-related changes to product labeling and provided the FDA with expanded authority to require the adoption of a Risk Evaluation and Mitigation Strategy, or REMS, to assure safe use of the product candidates, either as a condition of product candidate approval or on the basis of new safety information. We anticipate that our μ-opioid receptor product candidates, if approved, will require a REMS, and it is possible that our other product candidates may require a REMS. The REMS may include medication guides for patients, special communication plans to health care professionals or elements to assure safe uses such as restricted distribution methods, patient registries and/or other risk minimization tools. We cannot predict the specific REMS that will be required as part of the FDA's approval of our product candidates. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription, or dispensing of our product candidates, if approved. Depending on the extent of the REMS requirements, these requirements may significantly increase our costs to commercialize these product candidates and could negatively affect sales. Furthermore, risks of our product candidates that are not adequately addressed through proposed REMS for such product candidates also may prevent or delay their approval for commercialization.

Our μ-opioid receptor targeted product candidates, including OLINVO, may be classified as controlled substances, the making, use, sale, importation, exportation and distribution of which are subject to regulation by state, federal and foreign law enforcement and other regulatory agencies.

Our μ-opioid receptor targeted product candidates, including OLINVO, may be classified as controlled substances, which are subject to state, federal and foreign laws and regulations regarding their manufacture, use, sale, importation, exportation and distribution. Controlled substances are regulated under the Federal Controlled Substances Act of 1970, or CSA, and regulations of the DEA.

The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. Schedule I substances by definition have no established medicinal use and may not be marketed or sold in the United States. A pharmaceutical product may be listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest risk of abuse and Schedule V substances the lowest relative risk of abuse among such substances. We expect OLINVO to be regulated by the DEA as a Schedule II controlled substance.

Various states also independently regulate controlled substances. Though state controlled substances laws often mirror federal law, because the states are separate jurisdictions, they may separately schedule drugs as well. While some

states automatically schedule a drug when the DEA does so, in other states there must be rulemaking or a legislative action. State scheduling may delay commercial sale of any controlled substance drug product for which we obtain federal regulatory approval and adverse scheduling could impair the commercial attractiveness of such product. We or our collaborators must also obtain separate state registrations in order to be able to obtain, handle and distribute controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions from the states in addition to those from the DEA or otherwise arising under federal law.

For any of our product candidates classified as controlled substances, we and our suppliers, manufacturers, contractors, customers and distributors are required to obtain and maintain applicable registrations from state, federal and foreign law enforcement and regulatory agencies and comply with state, federal and foreign laws and regulations regarding the manufacture, use, sale, importation, exportation and distribution of controlled substances. There is a risk that DEA regulations may limit the supply of the compounds used in clinical trials for our product candidates, and, in the future, the ability to produce and distribute our products in the volume needed to both meet commercial demand and build inventory to mitigate possible supply disruptions.

Regulations associated with controlled substances govern manufacturing, labeling, packaging, testing, dispensing, production and procurement quotas, recordkeeping, reporting, handling, shipment and disposal. These regulations increase the personnel needs and the expense associated with development and commercialization of product candidates including controlled substances. The DEA, and some states, conduct periodic inspections of registered establishments that handle controlled substances. Failure to obtain and maintain required registrations or comply with any applicable regulations could delay or preclude us from developing and commercializing our product candidates containing controlled substances and subject us to enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate proceedings to revoke those registrations. In some circumstances, violations could lead to criminal proceedings. Because of their restrictive nature, these regulations could limit commercialization of any of our product candidates that are classified as controlled substances.

Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad.

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

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

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising, and promotional activities for such product, will be subject to ongoing requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration, and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The FDA also may impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our products for only their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

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

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. 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.

Our current and future relationships with customers and third party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers, physicians and third party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, which may constrain the business or financial arrangements and relationships through which we sell, market and distribute any drugs for which we obtain marketing approval. In addition, we may be subject to transparency

laws and patient privacy regulation by U.S. federal and state governments and by governments in foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs, such as Medicare and Medicaid;

- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government; the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose obligations on covered healthcare providers, health plans, and healthcare clearinghouses, as well as their business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Open Payments program, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to "payments or other transfers of value" made to physicians, which is defined to include doctors, dentists, optometrists, podiatrists and chiropractors, and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians and their immediate family members, requirements for manufacturers to submit reports to CMS by the 90th day of each calendar year, and subsequent disclosure of such information by CMS on a publicly available website; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which also could materially affect our business.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

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

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality, and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the PPACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the PPACA of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level beginning in 2014, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- the new requirements under the federal Open Payments program and its implementing regulations;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and will remain in effect through 2024 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. More recently, President Trump and the Republican Congressional leaders have vowed to repeal and replace PPACA. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, our financial operations.

It is possible that healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the reimbursement that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government healthcare 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.

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

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue, if any.

In some countries, particularly the countries of the European Union, 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. To obtain coverage and 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. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially

If we fail to comply with environmental, health, and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

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

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

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

Risks Related to Employee Matters and Managing Our Growth

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

We are highly dependent on the research, development, clinical, business development, legal, financial, and commercial expertise of our executive officers. Although we have entered into employment agreements with these individuals, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees.

Recruiting and retaining qualified management, scientific, clinical, manufacturing, sales and marketing, and other personnel also will be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific, clinical and commercial advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development, regulatory, manufacturing, sales, marketing, and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to continue to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs, manufacturing, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could expose us to liability and hurt our reputation.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct also could involve the improper use or misrepresentation of information obtained in the course of clinical trials, which could result in regulatory sanctions and 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 governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including the imposition of significant fines or other sanctions.

Other Risks Related to our Business

We intend to conduct a substantial portion of the clinical trials for our product candidates outside of the United States and, if approved, we intend to market our product candidates abroad through third party collaborators. Accordingly, we will be subject to the risks of doing business outside of the United States.

We intend to conduct a substantial portion of our clinical trials outside of the United States and, if approved, we intend to market our product candidates outside of the United States. We are thus subject to risks associated with doing business outside of the United States. With respect to our product candidates, we may choose to partner with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems outside of the United States or in lieu of our own sales force and distribution systems, which would indirectly expose us to these risks. Our business and financial results in the future could be adversely affected due to a variety of factors associated with conducting development and marketing of our product candidates, if approved, outside of the United States, including:

- efforts to develop an international sales, marketing and distribution organization may increase our expenses, divert our management's attention from the development of product candidates or cause us to forgo profitable licensing opportunities in these geographies;
- changes in a specific country's or region's political and cultural climate or economic condition;
- unexpected changes in foreign laws and regulatory requirements;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- inadequate intellectual property protection in foreign countries;
- trade-protection measures, import or export licensing requirements such as Export Administration Regulations promulgated by the U.S. Department of Commerce and fines, penalties or suspension or revocation of export privileges;
- regulations under the U.S. Foreign Corrupt Practices Act and similar foreign anti-corruption laws;
- the effects of applicable foreign tax structures and potentially adverse tax consequences; and
- significant adverse changes in foreign currency exchange rates which could make the cost of our clinical trials, to the extent conducted outside of the United States, more expensive.

Our business and operations would suffer in the event of system failures.

Despite our implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption to our product candidate development programs. For example, the loss of clinical trial data from completed, ongoing or planned 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 personal, confidential or proprietary information, we could incur liability and the further development of any of our product candidates could be delayed or abandoned.

Risks Related to Ownership of Our Common Stock

An active trading market for our common stock may not continue to develop or be sustained.

Although our common stock is listed on the NASDAQ Global Select Market, or NASDAQ, we cannot assure you that an active, liquid trading market for our shares will continue to develop or be sustained. If an active market for

our common stock does not continue to develop or is not sustained, it may be difficult for you to sell shares quickly or without depressing the market price for the shares or to sell your shares at all.

The trading price of the shares of our common stock has been and may continue to be volatile, and you may not be able to resell some or all of your shares at a desired price.

Since our common stock commenced trading in January 2014, our stock price has been highly volatile, with closing stock prices ranging from a high of $13.30 per share to a low of $3.81 per share. 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 in our stock 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:

- actual or anticipated variations in our operating results;
- changes in financial estimates by us or by any securities analysts who might cover our stock;
- the timing and results of our clinical trials for any of our product candidates;
- failure or discontinuation of any of our development programs;
- conditions or trends in our industry;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biopharmaceutical industry;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- capital commitments;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- announcements and expectations of additional financing efforts; and
- sales of our common stock, including sales by our directors and officers or specific stockholders.

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 the operation of our business.

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

The trading market for our common stock is influenced by the research and reports that equity research analysts publish about us and our business. As a relatively new 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. We have no 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.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. This could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. 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.

In addition, we have filed registration statements on Form S-8 registering the issuance of shares of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements on Form S-8 are available for sale in the public market subject to vesting arrangements and exercise of existing options, the grant of new options in the future, the lock-up agreements described above and the restrictions of Rule 144 in the case of our affiliates.

The issuance of additional stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other stockholders.

Our amended and restated certificate of incorporation authorizes us to issue up to 100,000,000 shares of common stock and up to 5,000,000 shares of preferred stock with such rights and preferences as may be determined by our board of directors. Subject to compliance with applicable rules and regulations, we may issue our shares of common stock or securities convertible into our common stock from time to time in connection with a financing, acquisition, investment, our stock incentive plans or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and cause the trading price of our common stock to decline.

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

We have incurred substantial losses during our history. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we may never achieve profitability. To the extent that we continue to generate tax losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Section 382 of the Internal Revenue Code of 1986, as amended, 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 may be limited. We have not completed our analysis to determine what, if any, impact any prior ownership change has had on our ability to utilize our net operating loss carryforwards. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As of December 31, 2016, we had federal net operating loss carryforwards of approximately $38.8 million that could be limited if we have experienced, or if in the future we experience, an ownership change.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our amended and restated certificate of incorporation and amended and restated bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by you and other stockholders. For example, our board of directors has the authority to issue up to 5,000,000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- only one of our three classes of directors will be elected each year;

- stockholders are not entitled to remove directors other than by a $66^{2}/_{3}\%$ vote and only for cause;
- stockholders are not permitted to take actions by written consent;
- stockholders cannot call a special meeting of stockholders; and
- stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

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

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 a majority of our outstanding common stock. As a result, these persons, acting together, would be able to control all matters requiring stockholder approval, including the election and removal of directors, the approval of any merger, consolidation, sale of all or substantially all of our assets, or other significant corporate transactions.

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

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earliest of (a) December 31, 2019, (b) the last day of the fiscal year in which we have total annual gross revenue of at least $1.0 billion, (c) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (d) any date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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, the Sarbanes-Oxley Act and the rules and regulations of NASDAQ. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal controls over financial reporting. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure

controls and procedures, are designed to prevent fraud. For our fiscal year ended December 31, 2016, we are obligated to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10-K filing for that year, as required by Section 404(a) of the Sarbanes-Oxley Act. We will continue to incur substantial additional professional fees and internal costs to expand our accounting and finance functions and expend significant management efforts. We may discover 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 error 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(a) of the Sarbanes-Oxley Act in a timely manner, or if we are unable to implement or 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. In addition, any testing by us conducted in connection with Section 404(a) of the Sarbanes-Oxley Act, or the subsequent testing by our independent registered public accounting firm conducted in connection with Section 404(b) of the Sarbanes-Oxley Act once we no longer qualify as an "emerging growth company," may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses; or may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement.

We are required to disclose changes made in our internal control procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an "emerging growth company" under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting pursuant to Section 404(b). We will cease to be an "emerging growth company" in 2017 if any of the following occur on or before December 31, 2017: (1) we generate $1.0 billion of annual revenue at an earlier date, (2) we issue more than $1.0 billion in non-convertible debt, or (3) we qualify as a large accelerated filer under SEC rules. If and when we cease to be an "emerging growth company," an assessment of the effectiveness of our internal controls by our independent registered public accounting firm will be very expensive and could detect problems that our management's assessment might not.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.

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 and have no plans to pay cash dividends in the foreseeable future. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of our term loan credit facility with Oxford Finance LLC and Pacific Western Bank prohibits us from paying cash 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.

We incur costs and demands upon management as a result of being a public company.

As a public company listed in the United States, we are incurring, and will continue to incur, significant legal, accounting and other costs, particularly after we cease to be an "emerging growth company." These costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and stock exchanges, may increase legal and financial compliance costs and make some activities more time consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If, notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules also might make it more difficult for us to obtain some types of insurance, including directors' and officers' liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our principal offices occupy approximately 16,714 square feet of leased office and laboratory space in King of Prussia, Pennsylvania pursuant to a lease agreement that expires in September 2020 and contains an early termination option effective at any time following May 31, 2018. In addition, we have leased approximately 2,600 square feet of office space in King of Prussia under a lease expiring on July 31, 2017 and vivarium space in Exton, Pennsylvania under an agreement expiring on December 31, 2018. In December 2016, we entered into a 130-month office lease for approximately 40,565 square feet of space in Wayne, Pennsylvania for our new principal executive office; the term for this lease is expected to commence in the third quarter of 2017. This lease also contains an exclusive option, exercisable until April 1, 2017, to lease up to an additional approximately 13,055 square feet of space at this location. We believe that our facilities are suitable and adequate to meet our current needs.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we are subject to litigation and claims arising in the ordinary course of business. We are not currently a party to any material legal proceedings and we are not aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results or financial condition.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

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

Market Information and Holders

Our common stock is traded on the NASDAQ Global Select Market under the symbol "TRVN." The following table sets forth, for the periods indicated, the high and low prices per share for our common stock as reported on the NASDAQ Global Select Market:

	High	Low
2016		
First quarter	$ 10.51	$ 6.55
Second quarter	$ 9.49	$ 5.58
Third quarter	$ 7.63	$ 6.13
Fourth quarter	$ 6.90	$ 3.76
2015		
First quarter	$ 8.16	$ 4.71
Second quarter	$ 7.80	$ 5.78
Third quarter	$ 13.57	$ 5.06
Fourth quarter	$ 13.02	$ 9.00

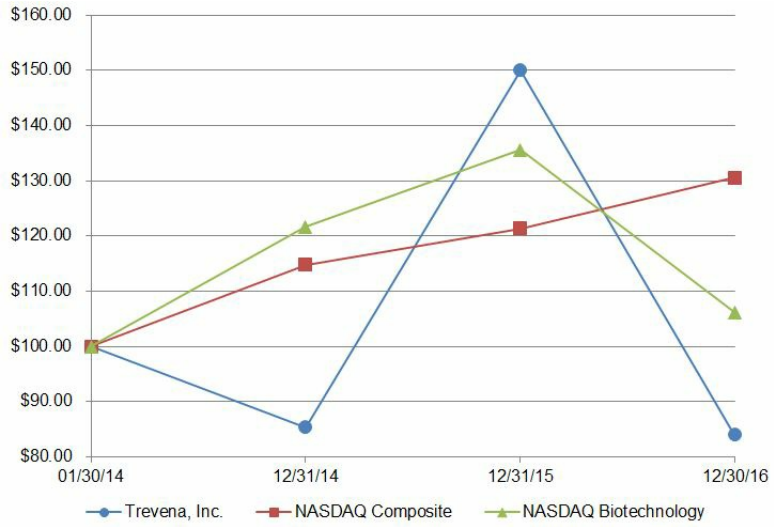
On March 3, 2017, there were 7 holders of record of our common stock and the closing price of our common stock was $4.17 per share.

Dividends

We have never declared or paid any dividends on our common stock. We anticipate that we will retain all of our future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying cash dividends in the foreseeable future. In addition, our ability to pay dividends, other than dividends payable solely in capital stock, is currently prohibited by the terms of our term loan credit facility with Oxford Finance, LLC and Pacific Western Bank.

Performance Graph

The following graph compares the performance of our common stock since January 30, 2014, the date preceding our initial public offering, or IPO, with the performance of the NASDAQ Composite and NASDAQ Biotechnology indexes. The comparison assumes a $100 investment on January 30, 2014 in our common stock at our IPO price, the stocks comprising the NASDAQ Composite index, and the stocks comprising the NASDAQ Biotechnology index, and assumes reinvestment of the full amount of all dividends, if any. Historical stockholder return is not necessarily indicative of the performance to be expected for any future periods.



The performance graph shall not be deemed to be incorporated by reference by means of any general statement incorporating by reference this Form 10-K into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent that we specifically incorporate such information by reference, and shall not otherwise be deemed filed under such acts.

Securities Authorized for Issuance under Equity Compensation Plans

The following table provides certain information with respect to all of our equity compensation plans in effect as of December 31, 2016:

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Issuance Under Equity Compensation Plans(1)(2)(3)
Equity compensation plans approved by stockholders	6,431,428	$ 6.12	1,327,137
Equity compensation plans not approved by stockholders	—	—	—
Total	6,431,428	$ 6.12	1,327,137

(1) Includes 225,806 shares of our common stock issuable under our 2013 Employee Stock Purchase Plan, or the 2013 ESPP. The number of shares of our common stock reserved for issuance under our 2013 ESPP will automatically increase on January 1 of each year, beginning on January 1, 2015 and continuing through and including January 1,

2023, by the number of shares equal to the least of (i) 225,806, (ii) the total number of shares of common stock issued under the 2013 ESPP during the immediately preceding calendar year, and (iii) such lower number of shares determined by our board of directors.

(2) Includes 1,101,331 shares of our common stock available for issuance under our 2013 Equity Incentive Plan. On January 1, 2015 and annually thereafter through January 1, 2023, the number of authorized shares under our 2013 Equity Incentive Plan will automatically increase by a number of shares equal to the lesser of: (i) 4% of the number of our shares issued and outstanding prior to the preceding December 31; or (ii) an amount determined by our Board of Directors.

(3) On December 15, 2016, our Board of Directors adopted the Trevena, Inc. Inducement Plan, or the Inducement Plan, which became effective on January 1, 2017, pursuant to which we reserved 500,000 shares of our common stock for issuance under the Inducement Plan. As the Inducement Plan was not effective on December 31, 2016, the shares are not included in this table.

ITEM 6. SELECTED FINANCIAL DATA

The following tables set forth our selected financial data for the periods indicated. The following statement of operations data for the years ended December 31, 2016, 2015 and 2014 and the selected balance sheet data as of December 31, 2016 and 2015 are derived from our audited financial statements appearing elsewhere in this report. The statement of operations data for the years ended December 31, 2013 and 2012, and the balance sheet data as of December 31, 2014, 2013, and 2012, have been derived from our audited financial statements that are not included herein.

This selected financial data should be read together with the historical financial statements and related notes to those statements, as well as "Management's Discussion and Analysis of Financial Condition and Results of Operations," which are included elsewhere in this report.

Our historical results are not necessarily indicative of the results that may be expected in the future, and our interim period results are not necessarily indicative of results to be expected for a full year or any other interim period.

	Year Ended December 31,				
	2016	2015	2014	2013	2012
Statement of Operations Data:	(in thousands, except share and per share data)				
Revenue					
Total revenue	$ 3,750	$ 6,250	$ —	$ 135	$ 808
Operating expenses:					
General and administrative	16,077	12,797	9,403	4,718	3,123
Research and development	89,956	44,074	40,547	18,762	13,295
Total operating expenses	106,033	56,871	49,950	23,480	16,418
Loss from operations	(102,283)	(50,621)	(49,950)	(23,345)	(15,610)
Total other income	(711)	93	249	94	(26)
Net loss	(102,994)	(50,528)	(49,701)	(23,251)	(15,636)
Accretion of redeemable convertible preferred stock	—	—	(29)	(334)	(316)
Net loss attributable to common stockholders	$ (102,994)	$ (50,528)	$ (49,730)	$ (23,585)	$ (15,952)
Net loss per share—basic and diluted	$ (1.97)	$ (1.15)	$ (2.02)	$ (29.71)	$ (23.70)
Weighted average shares of common stock outstanding used in computing net loss per share—basic and diluted	52,398,521	43,794,276	24,655,603	793,806	673,191

	As of December 31,				
	2016	2015	2014	2013	2012
	(in thousands)				
Balance Sheet Data:					
Cash and cash equivalents	$ 24,266	$ 46,774	$ 36,206	$ 37,965	$ 6,739
Marketable securities	86,335	125,864	70,699	—	—
Total assets	114,654	175,354	108,337	42,393	8,088
Total liabilities	36,073	32,223	9,134	3,401	8,127
Total redeemable convertible preferred stock	—	—	—	120,562	58,958
Total stockholders' equity (deficit)	78,581	143,131	99,204	(81,571)	(58,997)

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

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

Overview

Using our proprietary product platform, we have identified and are developing the following product candidates:

- *OLINVO™ (oliceridine injection):* We are developing OLINVO, a μ-receptor G protein pathway selective modulator (μ-GPS), for the management of moderate-to-severe acute pain where intravenous, or IV, administration is preferred. On February 21, 2017, we announced positive top-line results from our Phase 3 APOLLO-1 and APOLLO-2 pivotal efficacy studies of OLINVO in moderate-to-severe acute pain following bunionectomy and abdominoplasty, respectively. In both studies, all dose regimens achieved their primary endpoint of statistically greater analgesic efficacy than placebo, as measured by responder rate. The Phase 3 open-label ATHENA-1 safety study commenced in January 2016 and more than 400 patients have been treated in this study as of February 15, 2017. We have retained all worldwide development and commercialization rights to OLINVO, and plan to commercialize it in the United States for use in acute care settings such as hospitals and ambulatory surgery centers if it receives regulatory approval.

- *TRV250:* We are developing TRV250, a G protein biased ligand targeting the δ-receptor, as a compound with a potential first-in-class, non-narcotic mechanism for the treatment of migraine. TRV250 also may have utility in a range of other central nervous system, or CNS, indications. Because TRV250 selectively targets the δ-receptor, we believe it will not have the addiction liability of conventional opioids or other μ-opioid related adverse effects like those seen with morphine or oxycodone. In the second quarter of 2017, we expect to commence a Phase I study of TRV250 in the United Kingdom in healthy volunteers.

In addition to the above product candidates, we identified and have completed the initial Phase 1 studies for TRV734, an orally administered new chemical entity expected to be used for first-line treatment of moderate-to-severe acute and chronic pain. We intend to continue to focus our efforts for TRV734 on securing a development and commercialization partner for this asset. We had also been developing TRV027 for the treatment of acute heart failure, or AHF. In May 2016, we announced that TRV027 did not meet either the primary or secondary endpoints of our Phase 2b (BLAST-AHF) clinical trial of the compound. In August 2016, Allergan plc (formerly Actavis plc and Forest Laboratories Holdings Limited), or Allergan, notified us of its decision to not exercise its exclusive option to license TRV027. We are seeking a partner to fund any future clinical testing of TRV027.

Since our incorporation in late 2007, our operations have included organizing and staffing our company, business planning, raising capital, and discovering and developing our product candidates. We have financed our operations primarily through private placements and public offerings of our equity securities and debt borrowings. As of December 31, 2016, we had an accumulated deficit of $285.6 million. Our net loss was $103.0 million, $50.5 million and $49.7 million for the years ended December 31, 2016, 2015 and 2014, respectively. Our ability to become and remain profitable depends on our ability to generate revenue or sales. We do not expect to generate significant revenue or sales unless and until we or a collaborator obtain marketing approval for and commercialize OLINVO, TRV250 or TRV734.

In September 2014, we announced we had entered into a $35.0 million senior secured tranched term loan credit facility with Oxford Finance LLC and Pacific Western Bank (formerly Square 1 Bank), of which we have drawn $18.5 million as of December 31, 2016. Based upon the positive results of the Phase 3 efficacy trials of OLINVO

announced in February 2017, we believe we are now eligible to draw an additional $10.0 million under the credit facility until March 31, 2017.

We expect to incur significant expenses and operating losses for the foreseeable future as we continue the development and clinical trials of, and seek regulatory approval for, our product candidates. If we obtain regulatory approval for OLINVO, we expect to incur significant expenses associated with the launch of this product. We will need to obtain substantial additional funding in connection with our continuing operations. We will seek to fund our operations through the sale of equity, debt financings or other sources, including potential additional collaborations. However, we may be unable to raise additional funds or enter into such other agreements when needed on favorable terms, or at all. If we fail to raise capital or enter into such other arrangements as, and when, needed, we may have to significantly delay, scale back or discontinue our research and development programs and/or any future commercialization efforts.

Option Agreement with Allergan plc

In May 2013, we entered into an agreement with Allergan, under which we granted to Allergan an exclusive option to license TRV027. We received no consideration upon the grant of the option to Allergan. In March 2015, we signed a letter agreement with Allergan pursuant to which Allergan paid us $10.0 million to fund the expansion of the Phase 2b trial of TRV027 in AHF from 500 patients to 620 patients. The $10.0 million received in March 2015 was recorded as deferred revenue. The collaboration revenue was recorded on a straight-line basis through the expected term of the trial and was fully recognized as of June 30, 2016. In August 2016, Allergan notified us of its decision to not exercise its option. As such, we have retained all rights to TRV027.

Senior Secured Tranched Term Loan Credit Facility

In September 2014, we entered into a loan and security agreement with Oxford Finance LLC and Pacific Western Bank, or the lenders, pursuant to which they agreed to lend us up to $35.0 million in a three-tranche series of term loans (Term Loans A, B, and C). Upon initially entering into the agreement, we borrowed $2.0 million under Term Loan A. On April 13, 2015, we amended the agreement with the lenders to change the draw period for Term Loan B. On December 23, 2015, we further amended the agreement with the lenders to, among other things, change the draw period for Term Loan C, modify the interest only period, and modify the maturity date of the loan. In December 2015, we borrowed the Term Loan B tranche of $16.5 million. Our ability to draw an additional $16.5 million under Term Loan C was subject to the satisfaction of one or more specified triggers related to the results of our Phase 2b clinical trial of TRV027. Although those triggers were not attained, in December 2016, we and the lenders modified the terms and conditions under which we could exercise an option to draw $10.0 million of Term Loan C. As modified, we may draw $10.0 million of Term Loan C no later than March 31, 2017 and upon the lender's receipt of (a) satisfactory evidence that each of the two Phase 3 efficacy trials of OLINVO (APOLLO-1 and APOLLO-2) have met their respective primary endpoints and (b) a certificate from us concerning the ongoing ATHENA open label safety study of OLINVO. Based upon the positive results of the Phase 3 efficacy trials of OLINVO announced in February 2017, we believe we are now eligible to draw $10.0 million of Term Loan C under the credit facility until March 31, 2017.

Borrowings under Terms Loans A and B accrue interest at a fixed rate of 6.50% per annum. The applicable interest rate for Term Loan C will be the greater of (i) 6.5% and (ii) the sum of (a) 6.0% and (b) the 30-day U.S. LIBOR rate as of the date that is three days prior to the funding date of Term Loan C. We are required to make payments of interest only on borrowings under the loan agreement on a monthly basis through and including January 1, 2018, after which payments of principal in equal monthly installments and accrued interest will be due until the loan matures on March 1, 2020. If during the period from October 4, 2016 to March 31, 2017 we have received net cash proceeds of at least $50.0 million from the sale of our equity securities or from a joint venture, collaboration or other strategic partnering transaction, the maturity date will be further extended to December 1, 2020.

We paid the lenders a facility fee of $0.2 million in connection with the execution of the original agreement and an immaterial amendment fee in connection with the execution of the second and third amendments to the agreement. Upon the last payment date of the amounts borrowed under the agreement, we will be required to pay a final payment fee equal to 6.6% of the aggregate amounts borrowed, which is further increased to 7.0% if during the period from October 4, 2016 to March 31, 2017 we have received net cash proceeds of at least $50.0 million from the sale of our equity securities or from a joint venture, collaboration or other strategic partnering transaction. In addition, if we repay Term Loan A and Term Loan B prior to the applicable maturity date, we will pay the Lenders a prepayment fee of 3.0%

of the total amount prepaid if the prepayment occurs prior to December 23, 2016, 2.0% of the total amount prepaid if the prepayment occurs between December 23, 2016 and December 23, 2017, and 1.0% of the total amount prepaid if the prepayment occurs on or after December 24, 2017.

Our obligations are secured by a first priority security interest in substantially all of our assets, other than intellectual property. In addition, we have agreed not to pledge or otherwise encumber our intellectual property, with specified exceptions.

We used a placement agent in connection with the agreement. We paid the agent $0.1 million upon execution of the agreement and $0.1 million upon our draw of Term Loan B.

In connection with entering into the original agreement, we issued to the lenders and placement agent warrants to purchase an aggregate of 7,678 shares of our common stock; warrants to purchase an aggregate of 5,728 shares remain outstanding as of December 31, 2016. These warrants are exercisable immediately and have an exercise price of $5.8610 per share. The warrants may be exercised on a cashless basis and will terminate on the earlier of September 19, 2024 or the closing of a merger or consolidation transaction in which we are not the surviving entity. In connection with draw of Term Loan B, we issued to the lenders and placement agent additional warrants to purchase an aggregate of 34,961 shares of our common stock. These warrants have substantially the same terms as those noted above, and have an exercise price of $10.6190 per share and an expiration date of December 23, 2025.

Critical Accounting Policies and Significant Judgments and Estimates

The preparation of our consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements, as well as the reported revenues and expenses during the reported periods. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

A summary of our significant accounting policies appears in the notes to our audited consolidated financial statements for the year ended December 31, 2016 included in this annual report on Form 10-K. However, we believe that the following accounting policies are important to understanding and evaluating our reported financial results, and we have accordingly included them in this discussion.

Research and Development

Research and development costs are charged to expense as incurred. These costs include, but are not limited to, employee-related expenses, including salaries, benefits and travel and stock based compensation of our research and development personnel; expenses incurred under agreements with contract research organizations and investigative sites that conduct clinical trials and preclinical studies; the cost of acquiring, developing and manufacturing clinical trial materials; other laboratory supplies; allocated facilities, depreciation and other expenses, which include rent and utilities; insurance; and costs associated with preclinical activities and regulatory operations.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information provided to us by our vendors with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.

As part of the process of preparing our financial statements, we are required to estimate our expenses resulting from our obligations under contracts with vendors, clinical research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. Our objective is to reflect the appropriate trial expenses in our financial statements by matching those expenses with the period in which services are performed and efforts are expended. We may account for these expenses according to the progress of the trial as measured by subject progression and the timing of various aspects of the trial. We determine accrual estimates through financial models taking into account discussion with applicable personnel and outside service providers as to the progress or state of consummation

of trials, or the services completed. During the course of a clinical trial, we adjust our clinical expense recognition if actual results differ from estimates. We make estimates of our accrued expenses as of each balance sheet date based on the facts and circumstances known to us at that time. Our clinical trial accruals are dependent upon the timely and accurate reporting of contract research organizations and other third party vendors. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in it reporting amounts that are too high or too low for any particular period. For the years ended December 31, 2016, 2015 and 2014, there were no material adjustments to our prior period estimates of accrued expenses for clinical trials.

Stock-Based Compensation

We have applied the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification Topic 718, *Compensation — Stock Compensation*, or ASC 718, to account for stock-based compensation for employees. We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant.

Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock-based awards as of their measurement date. We recognize stock-based compensation expense over the requisite service period, which is the vesting period of the award. Calculating the fair value of stock-based awards requires that we make highly subjective assumptions. We use the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that we make assumptions as to the volatility of our common stock, the fair value of our common stock on the measurement date, the expected term of our stock options, the risk free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield. Because of our limited operating history as a publicly traded entity, we utilize data from a representative group of publicly traded companies to estimate expected stock price volatility. We selected representative companies from the biopharmaceutical industry with characteristics similar to us. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment* as we do not have sufficient historical stock option activity data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no current intention of paying cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

Under ASC 718, we are also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from our estimates. In March 2016, the FASB issued ASU 2016-09, *Compensation — Stock Compensation* (Topic 718), or ASU 2016-09, which provides for improvements to employee share-based payment accounting. In connection with the early adoption of ASU 2016-09 in the quarter ended December 31, 2016, the Company elected an accounting policy to record forfeitures as they occur.

Recent Accounting Pronouncements

See Note 2, *Summary of Significant Accounting Policies,* to the consolidated financial statements included in Part II of this annual report on Form 10-K for information on recent accounting pronouncements.

JOBS Act

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, contains provisions that, among other things, reduce reporting requirements for an “emerging growth company.” As an emerging growth company, we have elected to not take advantage of the extended transition period afforded by the JOBS Act for the implementation of new or revised accounting standards and, as a result, will comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

Results of Operations
(in thousands, except per share data)

Comparison of Years Ended December 31, 2016 and 2015

	Year Ended December 31,		
	2016	2015	Change
Revenue:			
Collaboration revenue	$ 3,750	$ 6,250	$ (2,500)
Total revenue	3,750	6,250	(2,500)
Operating expenses:			
General and administrative	16,077	12,797	3,280
Research and development	89,956	44,074	45,882
Total operating expenses	106,033	56,871	49,162
Loss from operations	(102,283)	(50,621)	(51,662)
Other income (expense):			
Change in fair value of warrant liability	78	(70)	148
Miscellaneous income	222	174	48
Net (loss) gain on asset disposals	(16)	(8)	(8)
Interest income	743	331	412
Interest expense	(1,738)	(334)	(1,404)
Total other (expense) income	(711)	93	(804)
Net loss attributable to common stockholders	$ (102,994)	$ (50,528)	$ (52,466)

Revenue

To date, we have derived revenue principally from research grants and collaboration arrangements. In March 2015, we signed a letter agreement with Allergan pursuant to which Allergan paid us $10.0 million to fund the expansion of our Phase 2b trial of TRV027 from 500 patients to 620 patients. The collaboration revenue was recorded on a straight-line basis over the remaining period of the trial and was fully recognized as of June 30, 2016.

General and administrative expense

General and administrative expenses consist principally of salaries and related costs for administrative personnel, including stock-based compensation and travel expenses. Other general and administrative expenses include professional fees for legal, consulting and accounting services.

General and administrative expenses increased by $3.3 million, or 26%, for the year ended December 31, 2016 compared to the same period in 2015, primarily as a result of increased headcount and associated salary, bonus and stock compensation expenses, and market research expenditures.

Research and development expense

Research and development expenses consist primarily of costs incurred for research and the development of our product candidates. In addition, research and development expenses include salaries and related costs for our research and development personnel and stock-based compensation and travel expenses for such individuals.

Research and development costs are expensed as incurred and are tracked by discovery program and subsequently by product candidate once a product candidate has been selected for development. We record costs for some development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors.

Research and development expenses increased by $45.9 million, or 104%, from $44.1 million for the year ended December 31, 2015 to $90.0 million for the year ended December 31, 2016. The following table summarizes our research and development expenses (in thousands):

	Year Ended December 31,	
	2016	2015
Personnel-related costs	$ 12,499	$ 9,646
OLINVO	63,156	16,916
TRV027	6,890	11,851
TRV250	2,970	1,014
Other research and development	4,441	4,647
	$ 89,956	$ 44,074

The increase in research and development expenses during the year ended December 31, 2016 was primarily driven by (i) increased expenditures on the development of OLINVO including expenses associated with initiating our Phase 3 program in 2016 partially offset by a decrease in expenses primarily associated with the completion of the OLINVO Phase 2b abdominoplasty clinical trial in 2015, (ii) the initiation of TRV250 IND-enabling studies during 2016, and (iii) increased headcount and associated salary, benefits and stock based compensation expense, all partially offset by (iv) decreased expenditures on the development of TRV027 due to the completion of the Phase 2b study in June 2016.

Other Income (Expense)

Other expense increased during the year ended December 31, 2016 primarily due to interest expense related to our Term Loan B tranche of $16.5 million that was drawn in December 2015.

Comparison of Years Ended December 31, 2015 and 2014

	Year Ended December 31,		
	2015	2014	Change
Revenue:			
Collaboration revenue	$ 6,250	$ —	$ 6,250
Total revenue	6,250	—	6,250
Operating expenses:			
General and administrative	12,797	9,403	3,394
Research and development	44,074	40,547	3,527
Total operating expenses	56,871	49,950	6,921
Loss from operations	(50,621)	(49,950)	(671)
Other income (expense):			
Change in fair value of warrant liability	(70)	122	(192)
Miscellaneous income	174	185	(11)
Net (loss) gain on asset disposals	(8)	(4)	(4)
Interest income	331	17	314
Interest expense	(334)	(71)	(263)
Total other (expense) income	93	249	(156)
Net loss	(50,528)	(49,701)	(827)
Accretion of preferred stock	—	(29)	29
Net loss attributable to common stockholders	$ (50,528)	$ (49,730)	$ (798)

Revenue

Collaboration revenue increased $6.2 million for the year ended December 31, 2015, as compared to the same period in 2014 as a result of entering into the letter agreement with Allergan on March 5, 2015 under which Allergan paid us $10.0 million to fund the expansion of our Phase 2b trial of TRV027 from 500 patients to 620 patients. The

collaboration revenue was recognized on a straight-line basis through the remaining period of the trial and was fully recognized as of June 30, 2016.

General and administrative expense

General and administrative expenses increased by $3.4 million, or 36%, for the year ended December 31, 2015 compared to the same period in 2014, primarily as a result of increased headcount and associated salary, bonus and stock compensation expenses, recruiting fees, and market research expenditures.

Research and development expense

Research and development expenses increased by $3.5 million, or 9%, from $40.5 million for the year ended December 31, 2014 to $44.1 million for the year ended December 31, 2015. The following table summarizes our research and development expenses (in thousands):

	Year Ended December 31,	
	2015	2014
Personnel-related costs	$ 9,646	$ 6,819
OLINVO	16,916	14,523
TRV027	11,851	11,792
Other research and development	5,661	7,413
	$ 44,074	$ 40,547

The increase for the year ended December 31, 2015 was primarily due to (i) increased headcount and associated salary, benefit and bonus expense and (ii) increased expenditures during 2015 on OLINVO including expenses associated with the Phase 2b abdominoplasty study clinical trial and product development costs, including the cost of clinical trial supplies. These increases were partially offset by decreases in expenditures associated with the Phase 1 program for TRV734.

Liquidity and Capital Resources
(in thousands, except per share data)

We incurred net losses of $103.0 million, $50.5 million and $49.7 million for the years ended December 31, 2016, 2015 and 2014, respectively. Net cash used in operating activities was $91.6, $40.1 million and $39.8 million during the years ended December 31, 2016, 2015 and 2014, respectively. At December 31, 2016, we had an accumulated deficit of $285.6 million, working capital of $90.3 million, cash and cash equivalents of $24.3 million, and marketable securities of $86.3 million.

Cash Flows

The following table summarizes our cash flows (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Net cash (used in) provided by:			
Operating activities	$ (91,554)	$ (40,075)	$ (39,778)
Investing activities	37,798	(56,939)	(71,157)
Financing activities	32,329	107,582	109,176
Net (decrease) increase in cash and cash equivalents	$ (21,427)	$ 10,568	$ (1,759)

Net cash used in operating activities

Net cash used in operating activities was $91.6 million for the year ended December 31, 2016 and consisted primarily of a net loss of $103.0 million and net cash outflows from a decrease in deferred revenue of $3.8 million. These cash outflows were partially offset by non-cash expense for stock compensation of $5.9 million, an increase in

accounts payable and accrued expenses of $7.1 million primarily associated with the Phase 3 OLINVO clinical trials, and other non-cash adjustments in our net loss totaling $2.2 million.

Net cash used in operating activities was $40.1 million for the year ended December 31, 2015, consisting primarily of a net loss of $50.5 million partially offset by noncash adjustments of $5.1 million and changes in operating assets and liabilities of $5.3 million. Changes in operating assets and liabilities were primarily driven by an increase of deferred revenue of $3.8 million associated with the payment received from Allergan in March 2015 and an increase in accounts payable and accrued expenses of $2.8 million, partially offset by a decrease in prepaid expenses and other assets of $1.2 million.

Net cash used in operating activities was $39.8 million for the year ended December 31, 2014, consisting primarily of a net loss of $49.7 million partially offset by noncash adjustments of $2.5 million and changes in operating assets and liabilities of $7.4 million. The noncash adjustments were primarily attributable to increased expense associated with stock options granted and depreciation and amortization related to leasehold improvements and capital equipment partially offset by a gain recognized on the revaluation of the warrant liability. Changes in operating assets and liabilities were driven by a decrease in prepaid expenses and other assets of $3.2 million and an increase in accounts payable and accrued expenses of $4.2 million. The decrease in prepaid expenses and other assets was primarily due to prepaid IPO costs incurred in 2013 partially offset by prepaid expenses in 2014 related to our Phase 2b clinical trial for TRV027 and our Phase 2a/b clinical trial for OLINVO. The increase in accounts payable and accrued expenses was primarily due to the timing and volume of our payment of costs related to ongoing development of our product candidates.

Net cash provided by (used in) investing activities

Net cash provided by investing activities for the year ended December 31, 2016 was $37.8 million. Net cash used in investing activities for the years ended December 31, 2015 and 2014 was $56.9 million and $71.2 million, respectively. Investing activities in all years consisted primarily of purchases and maturities of marketable securities as well as expenditures related to leasehold improvements and the purchase of capital equipment.

Net cash provided by financing activities

Net cash provided by financing activities was $32.3 million for the year ended December 31, 2016, which was primarily due to net proceeds of $32.1 million from the sale of common stock in February and December 2016 through an at-the-market, or ATM, sales facility with Cowen and Company, LLC, or Cowen.

Net cash provided by financing activities was $107.6 million for the year ended December 31, 2015, which was primarily due to net proceeds of $68.3 million from the public follow-on offering of common stock, net proceeds of $22.0 million from the sale of common stock through Cowen pursuant to the ATM sales facility and $16.4 million of net proceeds from our December 23, 2015 borrowing under our term loan agreement with Oxford Finance LLC and Pacific Western Bank.

Net cash provided by financing activities was $109.2 million for the year ended December 31, 2014, which was primarily due to net proceeds from the issuance of common stock in our IPO and our follow-on offering, as well as net proceeds from our initial borrowing under our term loan agreement on September 19, 2014 with Oxford Finance LLC and Pacific Western Bank.

All periods presented also include proceeds from exercises of common stock options.

Operating and Capital Expenditure Requirements

We have not achieved profitability since our inception and we expect to continue to incur net losses and negative cash flows from operations for the foreseeable future. We expect our cash expenditures to increase in the near term as we continue to fund our Phase 3 clinical program for OLINVO and prepare for commercialization of this product candidate, and initiate clinical development of TRV250. Additionally, if and when we believe a regulatory approval of a product candidate appears likely, we anticipate that our payroll and other general and administrative expenses will increase as we prepare for commercial operations, particularly with respect to expenses associated with the selling and marketing of any future products.

We believe that our cash and cash equivalents and marketable securities as of December 31, 2016, together with interest thereon, will be sufficient to fund our operating expenses and capital expenditure requirements into the second quarter of 2018. We anticipate that we will need to raise substantial additional financing in the future to fund our operations. To meet these requirements, we may draw down an additional $10.0 million under the credit facility and also seek to sell equity or convertible securities in public or private transactions that may result in dilution to our stockholders. In December 2015, we filed a $250 million shelf registration statement that includes a $75 million ATM sales facility with Cowen acting as our sales agent. Approximately $34.9 million remained available under the ATM sales facility as of March 1, 2017. We may offer and sell shares of our common stock under the existing registration statement (including under our ATM facility) or any registration statement we may file in the future. If we raise additional funds through the issuance of convertible securities, these securities could have rights senior to those of our common stock and could contain covenants that restrict our operations.

Ultimately, there can be no assurance that we will be able to obtain additional equity or debt financing on terms acceptable to us, if at all. Our future capital requirements will depend on many factors, including:

- the progress, timing and results of the Phase 3 program and NDA filing for OLINVO;
- our ability to enter into collaborative agreements for the development and commercialization of our product candidates, including, for example, OLINVO in regions outside the United States;
- the number and development requirements of any other product candidates that we may pursue;
- the scope, progress, results and costs of researching and developing our product candidates or any future product candidates, both in the United States and in territories outside the United States;
- the costs, timing and outcome of regulatory review of our product candidates or any future product candidates, both in the United States and in territories outside the United States;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- any product liability or other lawsuits related to our products;
- the expenses needed to attract and retain skilled personnel;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; and
- the costs involved in preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending our intellectual property-related claims, both in the United States and in territories outside the United States.

Please see “Risk Factors” for additional risks associated with our substantial capital requirements.

Contractual Obligations and Commitments

The following is a summary of our long-term contractual cash obligations as of December 31, 2016 (in thousands):

	Payments Due By Period				
	Total	Less than 1 year	1 - 3 years	3 - 5 years	More than 5 years
Operating lease obligations(1)	$ 13,044	$ 404	$ 2,387	$ 2,525	$ 7,728
Loans payable	18,500	5,139	12,334	1,027	—
Total	$ 31,544	$ 5,543	$ 14,721	$ 3,552	$ 7,728

(1) Operating lease obligations reflect our obligation to make payments in connection with the lease for our office spaces, including our current location in King of Prussia, Pennsylvania and our future location in Wayne, Pennsylvania.

Purchase Commitments

We have no material non-cancelable purchase commitments with contract manufacturers or service providers as we have generally contracted on a cancelable basis. In December 2016, we entered into a manufacturing agreement that is cancelable upon 24 months prior notice of cancellation.

License Agreements and Other Commitments

In the course of normal business operations, we have agreements with contract service providers to assist in the performance of our research and development and manufacturing activities. We can elect to discontinue the work under these agreements at any time. We also could enter into additional collaborative research, contract research, manufacturing and supplier agreements in the future, which may require upfront payments and even long-term commitments of cash.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements, as defined by applicable SEC regulations.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Our marketable securities consist of U.S. Treasury and U.S. government agency securities. The market value of such instruments fluctuates with current market interest rates. In general, as rates increase, the market value of a debt instrument would be expected to decrease; the opposite also is true. To minimize market risk, we have in the past held and, to the extent possible, will continue in the future to hold, such debt instruments to maturity at which time the debt instrument will be redeemed at its stated, or face, value. Due to the relatively short duration and nature of these instruments, we do not believe that we have a material exposure to interest rate risk related to our investment portfolio. Our marketable securities at December 31, 2016 totaled $86.3 million, and the weighted-average yield-to-maturity was approximately 0.7% with maturities of investments ranging up to 12 months.

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ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

REPORT OF MANAGEMENT

Management's Report on Financial Statements

Our management is responsible for the preparation, integrity and fair presentation of information in our financial statements, including estimates and judgments. The financial statements presented in this Annual Report on Form 10-K have been prepared in accordance with accounting principles generally accepted in the United States of America. Our management believes the financial statements and other financial information included in this Annual Report on Form 10-K fairly present, in all material respects, our financial condition, results of operations and cash flows as of and for the periods presented in this Annual Report on Form 10-K. The financial statements have been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report, which is included herein.

Management's Report on Internal Control Over Financial Reporting

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

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

Our management, including our Chief Executive Officer and Chief Financial Officer, do not expect that our internal control over financial reporting will prevent all error and all fraud. A control system, no matter how well designed and implemented, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues within a company are detected. The inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple errors or mistakes. Controls can also be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the controls. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and may not be detected.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2016. In making this assessment, our management used the criteria based on the framework set forth by the Committee of Sponsoring Organizations of the Treadway Commission in "Internal Control—Integrated Framework" (COSO). Based on our assessments we believe that, as of December 31, 2016, our internal control over financial reporting is effective based on those criteria.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Trevena, Inc.

We have audited the accompanying balance sheets of Trevena, Inc. (the Company) as of December 31, 2016 and 2015, and the related statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Trevena, Inc. at December 31, 2016 and 2015, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania
March 8, 2017

TREVENA, INC.

Balance Sheets

(in thousands, except share and per share data)

	2016	2015
Assets		
Current assets:		
Cash and cash equivalents	$ 24,266	$ 46,774
Marketable securities	86,335	125,864
Prepaid expenses and other current assets	1,788	1,893
Total current assets	112,389	174,531
Property and equipment, net	1,059	696
Restricted cash	1,193	112
Intangible asset, net	13	15
Total assets	$ 114,654	$ 175,354
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 8,749	$ 6,750
Accrued expenses and other current liabilities	8,208	3,030
Current portion of loans payable, net	5,039	—
Deferred revenue	—	3,750
Deferred rent	52	44
Total current liabilities	22,048	13,574
Loans payable, net	13,270	18,186
Capital leases, net of current portion	18	8
Deferred rent, net of current portion	187	239
Warrant liability	75	153
Other long term liabilities	475	63
Total liabilities	36,073	32,223
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Common stock—$0.001 par value; 100,000,000 shares authorized, 55,768,414 and 50,802,603 shares issued and outstanding at December 31, 2016 and December 31, 2015, respectively	56	51
Preferred stock—$0.001 par value; 5,000,000 shares authorized, none issued or outstanding at December 31, 2016 and December 31, 2015	—	—
Additional paid-in capital	364,148	325,784
Accumulated deficit	(285,625)	(182,498)
Accumulated other comprehensive income (loss)	2	(206)
Total stockholders' equity	78,581	143,131
Total liabilities and stockholders' equity	$ 114,654	$ 175,354

See accompanying notes to financial statements.

TREVENA, INC.

Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Year Ended December 31,		
	2016	**2015**	**2014**
Revenue:			
Collaboration revenue	$ 3,750	$ 6,250	$ —
Total revenue	3,750	6,250	—
Operating expenses:			
General and administrative	16,077	12,797	9,403
Research and development	89,956	44,074	40,547
Total operating expenses	106,033	56,871	49,950
Loss from operations	(102,283)	(50,621)	(49,950)
Other income (expense):			
Change in fair value of warrant liability	78	(70)	122
Miscellaneous income	222	174	185
Net (loss) gain on asset disposals	(16)	(8)	(4)
Interest income	743	331	17
Interest expense	(1,738)	(334)	(71)
Total other (expense) income	(711)	93	249
Net loss	(102,994)	(50,528)	(49,701)
Accretion of redeemable convertible preferred stock	—	—	(29)
Net loss attributable to common stockholders	$ (102,994)	$ (50,528)	$ (49,730)
Other comprehensive income (loss), net:			
Unrealized gain (loss) on marketable securities	208	(187)	(19)
Other comprehensive income (loss)	208	(187)	(19)
Comprehensive loss	$ (102,786)	$ (50,715)	$ (49,749)
Per share information:			
Net loss per share of common stock, basic and diluted	$ (1.97)	$ (1.15)	$ (2.02)
Weighted average common shares outstanding, basic and diluted	52,398,521	43,794,276	24,655,603

See accompanying notes to financial statements.

TREVENA, INC.
Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity
For the Period From January 1, 2014 to December 31, 2016
(in thousands, except share data)

	Redeemable Convertible Preferred Stock									Stockholders' Equity					
										Common Stock					
	Series A		Series B		Series B-1		Series C								
	Number of Shares	Amount	Number of Shares	Amount	Number of Shares	Amount	Number of Shares	Amount	Total	Number of Shares	$0.001 Par Value	Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
Balance, January 1, 2014	25,074,999	$ 25,024	30,800,000	$ 30,779	4,750,000	$ 4,823	36,764,704	$ 59,936	$120,562	957,756	$ 1	$ 697	$ (82,269)	$ —	$ (81,571)
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	2,384	—	—	2,384
Exercise of stock options	—	—	—	—	—	—	—	—	—	186,682	—	112	—	—	112
Accretion of Series A, Series B/B-1 and Series C convertible preferred stock to its redemption value	—	2	—	1	—	24	—	2	29	—	—	(28)	—	—	(28)
Conversion of Series A convertible preferred stock to common stock upon initial public offering	(25,074,999)	(25,026)	—	—	—	—	—	—	(25,026)	4,044,354	4	25,022	—	—	25,026
Conversion of Series B convertible preferred stock to common stock upon initial public offering	—	—	(30,800,000)	(30,780)	—	—	—	—	(30,780)	4,967,741	5	30,774	—	—	30,779
Conversion of Series B-1 convertible preferred stock to common stock upon initial public offering	—	—	—	—	(4,750,000)	(4,847)	—	—	(4,847)	766,129	1	4,846	—	—	4,847
Conversion of Series C convertible preferred stock to common stock upon initial public offering	—	—	—	—	—	—	(36,764,704)	(59,938)	(59,938)	5,929,789	6	59,932	—	—	59,938
Net conversion of preferred stock warrants common stock upon initial public offering	—	—	—	—	—	—	—	—	—	20,273	—	—	—	—	—
Reclassification of convertible preferred stock warrant liability	—	—	—	—	—	—	—	—	—	—	—	145	—	—	145
Issuance of common stock warrants	—	—	—	—	—	—	—	—	—	—	—	1	—	—	1
Issuance of common stock, net of issuance costs	—	—	—	—	—	—	—	—	—	22,368,449	22	107,268	—	—	107,290
Change in unrealized loss on marketable securities	—	—	—	—	—	—	—	—	—	—	—	—	—	(19)	(19)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(49,701)	—	(49,701)
Balance, December 31, 2014	—	—	—	—	—	—	—	—	—	39,241,173	39	231,153	(131,970)	(19)	99,203
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	3,427	—	—	3,427
Exercise of stock options	—	—	—	—	—	—	—	—	—	384,033	1	905	—	—	906
Net exercise of common stock warrant	—	—	—	—	—	—	—	—	—	2,397	—	—	—	—	—
Issuance of common stock warrants	—	—	—	—	—	—	—	—	—	—	—	4	—	—	4
Issuance of common stock, net of issuance costs	—	—	—	—	—	—	—	—	—	11,175,000	11	90,295	—	—	90,306
Unrealized loss on marketable securities	—	—	—	—	—	—	—	—	—	—	—	—	—	(187)	(187)
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(50,528)	—	(50,528)
Balance, December 31, 2015	—	$ —	—	$ —	—	$ —	—	$ —	$ —	50,802,603	$ 51	$ 325,784	$ (182,498)	$ (206)	$ 143,131
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	5,903	—	—	5,903
Exercise of stock options	—	—	—	—	—	—	—	—	—	149,622	—	256	—	—	256
Net exercise of common stock warrant	—	—	—	—	—	—	—	—	—	698	—	—	—	—	—
Issuance of common stock, net of issuance costs	—	—	—	—	—	—	—	—	—	4,815,491	5	32,072	—	—	32,077
Unrealized gain on marketable securities	—	—	—	—	—	—	—	—	—	—	—	—	—	208	208
Adjustment to accumulated deficit as a result of adoption of ASU 2016-09	—	—	—	—	—	—	—	—	—	—	—	133	(133)	—	—
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	(102,994)	—	(102,994)
Balance, December 31, 2016	—	$ —	—	$ —	—	—	—	—	$ —	55,768,414	$ 56	$ 364,148	$ (285,625)	$ 2	$ 78,581

See accompanying notes to financial statements.

TREVENA, INC.

Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2016	2015	2014
Operating activities:		(in thousands)	
Net loss	$ (102,994)	$ (50,528)	$ (49,701)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	246	208	239
Stock-based compensation	5,903	3,427	2,383
Noncash interest expense on loans	534	180	33
Loss on disposal of assets	17	11	5
Revaluation of warrant liability	(78)	70	(122)
Amortization of bond premiums on marketable securities	1,334	1,210	—
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	104	(1,224)	3,197
Accounts payable and accrued expenses	7,130	2,821	4,188
Deferred revenue	(3,750)	3,750	—
Net cash used in operating activities	(91,554)	(40,075)	(39,778)
Investing activities:			
Purchases of property and equipment	(605)	(361)	(440)
Purchase of intangible asset	—	(15)	—
Maturities of marketable securities	115,824	69,827	—
Purchases of marketable securities	(77,421)	(126,390)	(70,717)
Net cash provided by (used in) investing activities	37,798	(56,939)	(71,157)
Financing activities:			
Proceeds from exercise of common stock options	256	906	112
Proceeds from loans payable, net	—	16,368	1,775
Proceeds from issuance of common stock, net	32,077	90,311	107,290
Capital lease payments	(4)	(3)	(1)
Net cash provided by financing activities	32,329	107,582	109,176
Net (decrease) increase in cash and cash equivalents	(21,427)	10,568	(1,759)
Cash, cash equivalents, and restricted cash—beginning of period	46,886	36,318	38,077
Cash, cash equivalents, and restricted cash—end of period	$ 25,459	$ 46,886	$ 36,318
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 1,204	$ 155	$ 37
Capital lease additions	$ 18	$ —	$ 14
Fair value of common stock warrants issued	$ —	$ 4	$ 1

See accompanying notes to financial statements.

TREVENA, INC.

Notes to Financial Statements

December 31, 2016

1. Organization and Description of the Business

Trevena, Inc., or the Company, was incorporated in Delaware as Parallax Therapeutics, Inc. on November 9, 2007. The Company began operations in December 2007, and its name was changed to Trevena, Inc. on January 3, 2008. The Company is a biopharmaceutical company developing innovative therapies based on breakthrough science to benefit patients and healthcare providers confronting serious medical conditions. The Company operates in one segment and has its principal office in King of Prussia, Pennsylvania.

Liquidity

At December 31, 2016, the Company had an accumulated deficit of $285.6 million. The Company's net loss was $103.0 million, $50.5 million and $49.7 million for the years ended December 31,2016, 2015 and 2014, respectively. The Company expects its cash and cash equivalents of $24.3 million and marketable securities of $86.3 million as of December 31, 2016, together with interest thereon, to be sufficient to fund its operating expenses and capital expenditure requirements into the second quarter of 2018.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America, or GAAP. Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification, or ASC, and Accounting Standards Update, or ASU, of the Financial Accounting Standards Board, or FASB. The Company's functional currency is the U.S. dollar.

Use of Estimates

Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether potentially reasonable estimates of the ultimate future outcomes and management must select an amount that falls within that range of reasonable estimates. This process may result in actual results differing materially from those estimated amounts used in the preparation of the financial statements if these results differ from historical experience, or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. In preparing these financial statements, management used significant estimates in the following areas, among others: stock-based compensation expense, the determination of the fair value of stock-based awards, the fair value of liability-classified common stock warrants, and the accounting for research and development costs, accrued expenses and the recoverability of the Company's net deferred tax assets and related valuation allowance. The financial data and other information disclosed in these notes are not necessarily indicative of the results to be expected for any future year or period.

Cash and Cash Equivalents and Marketable Securities

The Company considers all highly liquid investments that have maturities of three months or less when acquired to be cash equivalents. Cash equivalents are valued at cost, which approximates their fair market value. The Company maintains a portion of its cash and cash equivalent balances in money market mutual funds that invest substantially all of their assets in U.S. government agency securities, U.S. Treasury securities and reverse repurchase agreements, or RRAs. RRAs are collateralized by deposits in the form of 'Government Securities and Obligations' for an

amount not less than 102% of their value. The Company does not record an asset or liability related to the collateral, as the Company is not permitted to sell or repledge the associated collateral.

The Company maintains its marketable securities balances in the form of U.S. Treasury and U.S. government agency securities. The Company classifies its marketable securities as "available-for-sale", pursuant to ASC Topic 320, *Investments—Debt and Equity Securities*, or ASC 320, carries them at fair market value and classifies them as current assets on its balance sheets. Unrealized gains and losses on marketable securities are recorded as a separate component of accumulated other comprehensive income/(loss) included in stockholders' equity. As of December 31, 2016 and 2015, the Company had $86.3 million and $125.9 million, respectively, in available-for-sale investments, all classified as current assets. See Note 3 for additional information.

The fair value of the Company's investments is determined based on observable market quotes or valuation models using assessments of counterparty credit worthiness, credit default risk of underlying security and overall capital market liquidity. The Company reviews unrealized losses associated with available-for-sale securities to determine the classification as "temporary" or "other-than-temporary" impairment. A temporary impairment results in an unrealized loss being recorded in other comprehensive income (loss). If a decline in the fair value is considered other-than-temporary, based on available evidence, the unrealized loss is transferred from other comprehensive income (loss) to the statement of operations. The Company considers various factors in determining the classification, including the length of time and extent to which the fair value has been less than the Company's cost basis, the financial condition and near-term prospects of the issuer or investee, and the Company's ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in market value. Realized gains (losses) are included in interest income (expense) in the statement of operations and comprehensive income (loss) on a specific identification basis.

Restricted Cash

The Company maintains $1.1 million as collateral under a letter of credit for the Company's new facility lease obligations in Wayne, Pennsylvania. The Company also maintains a letter of credit totaling $0.1 million as collateral for the Company's facility lease obligations in King of Prussia, Pennsylvania. The Company has recorded these deposits and accumulated interest thereon as restricted cash on its balance sheet.

Fair Value of Financial Instruments

The carrying amount of the Company's financial instruments, which include cash and cash equivalents, marketable securities, restricted cash, accounts payable and accrued expenses approximate their fair values, given their short-term nature. The carrying amount of the Company's loans payable at December 31, 2016 and 2015 is the nominal value of the loan payable, which is the carrying value, net of debt discount and deferred charges. The nominal value approximates fair value because the interest rate is reflective of the rate the Company could obtain on debt with similar terms and conditions. Certain of the Company's common stock warrants are carried at fair value, as disclosed below.

The Company has evaluated the estimated fair value of financial instruments using available market information and management's estimates. The use of different market assumptions and/or estimation methodologies could have a significant effect on the estimated fair value amounts. See Note 3 for additional information.

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's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk. The Company has no off-balance sheet concentrations of credit risk such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Property and Equipment

Property and equipment consists of computer and laboratory equipment, software, office equipment, furniture, manufacturing equipment and leasehold improvements and is recorded at cost. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, retirement or sale, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is

included in the results of operations. Property and equipment are depreciated on a straight-line basis over their estimated useful lives. The Company uses a life of three years for computer equipment and five years for laboratory equipment, office equipment, furniture, manufacturing equipment and software. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset.

The Company reviews long-lived assets when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparison of the book values of the assets to future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book value of the assets exceed their fair value, which is measured based on the projected discounted future net cash flows arising from the assets. No impairment losses have been recorded since inception.

Intangible Asset

Identifiable intangible assets are initially recorded at fair market value at the time of acquisition, utilizing a cost approach and the initial value is amortized over the expected useful life of the asset. The Company also capitalizes costs incurred to renew or extend the term of recognized intangible assets.

In 2015, the Company recorded an immaterial intangible asset related to the Company website and expects to recognize amortization in proportional amounts over each of the next eight years. Amortization expense on intangible assets was immaterial for the years ended December 31, 2016 and 2015.

The determination of the value of intangible assets requires management to make estimates and assumptions that affect the Company's consolidated financial statements. The Company assesses potential impairments to intangible assets when there is evidence of events or changes in circumstances that indicate the carrying amount of an asset may not be recovered. The Company's judgements regarding the existence of impairment indicators and future cash flows related to intangible assets are based on operational performance of the Company, market conditions and other factors. If impairment is indicated, the Company will reduce the carrying value of the intangible assets to fair value. The Company believes the future cash flows to be received from its intangible asset will exceed the intangible asset carrying value, and accordingly, the Company has not recognized any impairment losses through December 31, 2016.

Common Stock Warrants

Freestanding warrants that are related to the purchase of common stock are classified as liabilities and recorded at fair value regardless of the timing of the redemption feature or the redemption price or the likelihood of redemption. The warrants are subject to re-measurement at each balance sheet date and any change in fair value is recognized as a component of change in fair value of warrant liability in the statements of operations and comprehensive loss. The Company will continue to adjust the liability for changes in fair value until the earlier of the exercise or expiration of the warrants. The warrants are classified as Level 3 liabilities (see Note 3 for additional information).

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the chief executive officer. The Company and the chief executive officer view the Company's operations and manage its business as one operating segment. All long-lived assets of the Company reside in the United States.

Revenue

The Company recognizes collaboration revenue when persuasive evidence of an arrangement exists, delivery has occurred or services have been rendered, the price is fixed and determinable, and collectibility is reasonably assured.

Research and Development

Research and development costs are charged to expense as incurred. These costs include, but are not limited to, employee-related expenses, including salaries, benefits and travel and stock-based compensation of the Company's

research and development personnel; expenses incurred under agreements with contract research organizations and investigative sites that conduct clinical trials and preclinical studies; the cost of acquiring, developing and manufacturing clinical trial materials; other laboratory supplies; allocated facilities, depreciation and other expenses, which include rent and utilities; insurance; and costs associated with preclinical activities and regulatory operations.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as subject enrollment, clinical site activations or information provided to the Company by its vendors with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.

As part of the process of preparing its financial statements, the Company is required to estimate its expenses resulting from its obligations under contracts with vendors, clinical research organizations and consultants, and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. The Company's objective is to reflect the appropriate trial expenses in its financial statements by matching those expenses with the period in which services are performed and efforts are expended. The Company may account for these expenses according to the progress of the trial as measured by subject progression and the timing of various aspects of the trial. The Company determines accrual estimates through financial models taking into account discussion with applicable personnel and outside service providers as to the progress or state of consummation of trials, or the services completed. During the course of a clinical trial, the Company adjusts its clinical expense recognition if actual results differ from its estimates. The Company makes estimates of its accrued expenses as of each balance sheet date based on the facts and circumstances known to it at that time. The Company's clinical trial accruals are dependent upon the timely and accurate reporting of contract research organizations and other third party vendors. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in it reporting amounts that are too high or too low for any particular period. For the years ended December 31, 2016, 2015 and 2014, there were no material adjustments to the Company's prior period estimates of accrued expenses for clinical trials.

Stock-Based Compensation

At December 31, 2016, the Company had one stock-based compensation plan, which is more fully described in Note 7. The Company has applied the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification Topic 718, *Compensation — Stock Compensation*, to account for stock-based compensation for employees. The Company recognizes compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant.

Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock-based awards as of their measurement date. The Company recognizes stock-based compensation expense over the requisite service period, which is the vesting period of the award. Calculating the fair value of stock-based awards requires that the Company makes highly subjective assumptions. The Company uses the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that the Company makes assumptions as to the volatility of its common stock, the fair value of its common stock on the measurement date, the expected term of its stock options, the risk free interest rate for a period that approximates the expected term of its stock options and its expected dividend yield. Because of the Company's limited operating history as a publicly traded entity, the Company utilizes data from a representative group of publicly traded companies to estimate expected stock price volatility. The Company selected representative companies from the biopharmaceutical industry with characteristics similar to the Company. The Company use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, as the Company does not have sufficient historical stock option activity data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends and has no current intention of paying cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

Under ASC 718, the Company is also required to estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from the Company's estimates. In March 2016, the FASB

issued ASU 2016-09, *Compensation — Stock Compensation* (Topic 718), or ASU 2016-09, which provides for improvements to employee share-based payment accounting. The Company early adopted ASU 2016-09 as of December 31, 2016. In connection with the early adoption, the Company elected an accounting policy to record forfeitures as they occur. See Note 14.

See Note 7 for a discussion of the assumptions used by the Company in determining the grant date fair value of options granted under the Black-Scholes option pricing model, as well as a summary of the stock option activity under the Company's stock-based compensation plan for all years presented.

Income Taxes

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes*, or ASC 740, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position, as well as consideration of the available facts and circumstances. To date, the Company has not taken any uncertain tax position or recorded any reserves, interest or penalties.

Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss relates to unrealized investment losses on the Company's marketable securities for all periods presented.

Basic and Diluted Net Loss Per Share of Common Stock

Basic net 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 the period, excluding the dilutive effects of preferred stock, warrants to purchase preferred stock and stock options. Diluted net loss per share of common stock is computed by dividing the net loss attributable to common stockholders by the sum of the weighted-average number of shares of common stock outstanding during the period plus the potential dilutive effects of preferred stock and warrants to purchase preferred stock, and stock options outstanding during the period calculated in accordance with the treasury stock method, although these shares, options and warrants are excluded if their effect is anti-dilutive. Because the impact of these items is anti-dilutive during periods of net loss, there was no difference between basic and diluted net loss per share of common stock for all periods presented.

Recently Adopted Accounting Standards

In November 2016, FASB issued ASU 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash*, or ASU 2016-18, which clarifies the presentation of restricted cash and restricted cash equivalents in the statements of cash flows. Under ASU 2016-18 restricted cash and restricted cash equivalents are included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statements of cash flows. The Company adopted ASU 2016-18 during the three months ended December 31, 2016 on a retrospective basis. As a result, beginning-of-period cash, cash equivalents and restricted cash in the statement of cash flows increased by $0.1 million in 2016, 2015, and 2014.

In March 2016, the FASB issued ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting*, or ASU 2016-09, which amends ASC Topic 718, *Compensation—Stock Compensation*. ASU 2016-09 is designed to simplify several aspects of accounting for share-based payment award transactions that include the income tax consequences, classification of awards as either equity or liabilities, and classification of excess tax benefits on the

statement of cash flows. This guidance also permits an accounting policy election to either estimate the number of awards that are expected to vest or account for forfeitures when they occur. The Company elected to early adopt this standard during the three months ended December 31, 2016 and has elected to recognize forfeitures as they occur. The adoption did not have a material effect on the Company's interim and annual 2016 financial statements.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes*. The standard requires that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position. Entities are currently required to separate deferred income tax liabilities and assets into current and noncurrent amounts in a classified statement of financial position. The adoption of this standard did not have an impact on the Company's financial position or statements of operations.

In August 2014, the FASB issued ASU 2014-15, *Presentation of Financial Statements-Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASU 2104-15, which defines management's responsibility to assess an entity's ability to continue as a going concern, and to provide related footnote disclosures if there is substantial doubt about its ability to continue as a going concern within one year after the date that the financial statements are issued (or within one year after the date that the financial statements are available to be issued when applicable). This new rule requires management to assess an entity's ability to continue as a going concern by incorporating and expanding upon certain principles currently in the U.S. auditing standards. Based on the Company's analysis, the adoption of ASU 2014-15 as of December 31, 2016 did not have a material impact on the Company's consolidated financial statements or footnote disclosures, but may require additional disclosures in future periods.

Recent Accounting Standards Not Yet Adopted

In August 2016, the FASB issued ASU 2016-15, *Statement of Cash Flows (Topic 230),* or ASU 2016-15. ASU 2016-15 was issued to clarify how certain cash receipts and payments should be presented in the statement of cash flows. The standard is effective for annual periods beginning after December 15, 2017 and interim periods within that reporting period. Early adoption is permitted. The Company is evaluating the effect this standard will have on its financial statements and related disclosures.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842*), or ASU 2016-02. ASU 2016-02 requires lessees to record most leases on their balance sheets and disclose key information about leasing arrangements in an effort to increase transparency and comparability among organizations. The standard is effective for annual periods beginning after December 15, 2018 and interim periods within that reporting period. Early adoption is permitted. The Company is evaluating the effect this standard will have on its financial statements and related disclosures.

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers,* or ASU 2014-09. ASU 2014-09 is a comprehensive new revenue recognition model requiring a company to recognize revenue to depict the transfer of goods or services to a customer in an amount reflecting the consideration it expects to receive in exchange for those goods or services. Additionally, in March 2016, the FASB issued Accounting Standards Update 2016-08 *Revenue from Contracts with Customers, Principal versus Agent Considerations*, or ASU 2016-08. ASU 2016-08 amends the principal versus agent guidance in ASU 2014-09 to clarify how an entity should identify the unit of accounting for the principal versus agent evaluation and how it should apply the control principal to certain types of arrangements. The effective date for both standards is January 1, 2018, with an option that permits companies to adopt the standard as early as the January 1, 2017. Early application prior to the January 1, 2017 is not permitted. The standards permit the use of either the retrospective or cumulative effect transition method. The Company is evaluating the transition method that it will elect. The adoption of these standards is not expected to have a material impact on the Company's financial statement.

3. Fair Value of Financial Instruments

ASC Topic 820, *Fair Value Measurement,* or ASC 820, establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes among the following:

- Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access.
- Level 2—Valuations based on quoted prices for similar assets or liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active and models for which all significant inputs are observable, either directly or indirectly.
- Level 3—Valuations based on inputs that are unobservable and significant to the overall fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Cash, Cash Equivalents, Restricted Cash, and Marketable Securities

The following table presents the Company's cash, cash equivalents, restricted cash, and marketable securities as of December 31, 2016 and 2015 (in thousands):

	December 31, 2016						
	Adjusted Cost	Unrealized Gains	Unrealized Losses	Fair Value	Cash and Cash Equivalents	Restricted Cash	Marketable Securities
Cash	$ 13,756	$ —	$ —	$ 13,756	$ 12,563	$ 1,193	$ —
Level 1 (1):							
Money market funds	10,043	—	—	10,043	10,043	—	—
Level 2 (2):							
Cash and cash equivalents	1,660	—	—	1,660	1,660	—	—
U.S. government agency securities	86,333	19	(17)	86,335	—	—	86,335
Subtotal	87,993	19	(17)	87,995	1,660	—	86,335
Total	$ 111,792	$ 19	$ (17)	$ 111,794	$ 24,266	$ 1,193	$ 86,335

	December 31, 2015						
	Adjusted Cost	Unrealized Gains	Unrealized Losses	Fair Value	Cash and Cash Equivalents	Restricted Cash	Marketable Securities
Cash	$ 20,785	$ —	$ —	$ 20,785	$ 20,673	$ 112	$ —
Level 1 (1):							
Money market funds	4,101	—	—	4,101	4,101	—	—
U.S. Treasury securities	12,021	—	(1)	12,020	—	—	12,020
Subtotal	16,122	—	(1)	16,121	4,101	—	12,020
Level 2 (2):							
Repurchase agreements	22,000	—	—	22,000	22,000	—	—
U.S. government agency securities	114,049	—	(205)	113,844	—	—	113,844
Subtotal	136,049	—	(205)	135,844	22,000	—	113,844
Total	$ 172,956	$ —	$ (206)	$ 172,750	$ 46,774	$ 112	$ 125,864

(1) The fair value of Level 1 securities is estimated based on quoted prices in active markets for identical assets or liabilities.

(2) The fair value of Level 2 securities is estimated based on observable inputs other than quoted prices in active markets for identical assets and liabilities, quoted prices for identical or similar assets or liabilities in inactive markets, or other inputs that are observable or can be corroborated by observable market data for substantially the full term on the assets or liabilities.

The Company classifies investments available to fund current operations as current assets on its balance sheets. As of December 31, 2016, the Company did not hold any investment securities exceeding a one-year maturity.

Unrealized gains and losses on marketable securities are recorded as a separate component of accumulated other comprehensive income (loss) included in stockholders' equity. The Company recorded an unrealized gain of $0.2 million and an unrealized loss of $0.2 million during the years ended December 31, 2016 and 2015, respectively. Realized gains (losses) are included in interest income (expense) in the statement of operations and comprehensive income (loss) on a specific identification basis. The Company did not record any realized gains or losses during the years ended December 31, 2016 and 2015. To date, the Company has not recorded any impairment charges on marketable securities related to other-than-temporary declines in market value.

The Company recognizes transfers between levels of the fair value hierarchy as of the end of the reporting period. There were no transfers in or out of Level 3 in the hierarchy during the years ended December 31, 2016 or 2015.

Warrant Liability

At December 31, 2016, there is an outstanding warrant to purchase up to 20,161 shares of the Company's common stock with a fair value recorded as a liability as it contains a cash settlement feature upon certain strategic transactions. The following table sets forth a summary of changes in the fair value of this warrant liability, which

represents a recurring measurement that is classified within Level 3 of the fair value hierarchy, wherein fair value is estimated using significant unobservable inputs (in thousands):

	Warrant Liability
Balance as of January 1, 2015	$ 83
Amounts acquired or issued	—
Changes in estimated fair value	70
Balance as of December 31, 2015	153
Amounts acquired or issued	—
Changes in estimated fair value	(78)
Balance as of December 31, 2016	$ 75

On each re-measurement date, the fair value of the warrant classified as a liability is estimated using the Black-Scholes option pricing model. For this liability, the Company develops its own assumptions that do not have observable inputs or available market data to support the fair value. This method of valuation involves using inputs such as the fair value of the Company's common stock, stock price volatility, the contractual term of the warrants, risk-free interest rates and dividend yields. Due to the nature of these inputs, the valuation of the warrants is considered a Level 3 measurement. The following assumptions were used at December 31, 2016 and 2015 to determine the warrant liability:

	December 31,	
	2016	2015
Estimated remaining term	5.3 years	6.3 years
Risk-free interest rate	2.0%	2.0%
Volatility	77.2%	67.4%
Dividend yield	0%	0%
Fair value of underlying instrument*	$ 5.88	$ 10.50

* Trevena, Inc. closing stock price.

The warrant liability is recorded on its own line item on the Company's balance sheets and is marked-to-market at each reporting period with the change in fair value recorded on its own line in the statements of operations and comprehensive loss.

In addition to the outstanding warrant to purchase 20,161 shares of common stock discussed above, the Company has outstanding warrants to purchase an aggregate of 40,689 shares of the Company's common stock. These warrants qualify for equity classification and have been allocated upon the relative fair value of the base instrument and the warrants. See Note 6 for additional information.

4. Property and Equipment, net

Property and equipment consisted of the following (in thousands):

	Estimated Useful Life in Years	December 31,	
		2016	2015
Laboratory equipment	5	$ 1,935	$ 1,796
Computers and software	3 - 5	521	503
Office equipment and furniture	5	314	281
Manufacturing equipment	5	242	—
Leasehold improvements	5	2,150	2,062
Leased assets	5	32	14
Total property and equipment		5,194	4,656
Less accumulated depreciation and amortization		(4,135)	(3,960)
Property and equipment, net		$ 1,059	$ 696

Depreciation and amortization expense was $0.2 million for each of the years ended December 31, 2016, 2015 and 2014.

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31,	
	2016	2015
Compensation and benefits	$ 2,680	$ 2,600
Clinical trial expenses	5,479	401
Other accrued expenses and other current liabilities	49	29
Total accrued expenses and other current liabilities	$ 8,208	$ 3,030

6. Loans Payable

In September 2014, the Company entered into a loan and security agreement with Oxford Finance LLC and Pacific Western Bank (formerly Square 1 Bank), (together, "the lenders"), pursuant to which the lenders agreed to lend the Company up to $35.0 million in a three-tranche series of term loans (Term Loans A, B, and C). Upon initially entering into the agreement, the Company borrowed $2.0 million under Term Loan A. On April 13, 2015, the Company amended the agreement with the lenders to change the draw period for Term Loan B. On December 23, 2015, the Company further amended the agreement with the lenders to, among other things, change the draw period for Term Loan C, modify the interest only period, and modify the maturity date of the loan. In December 2015, the Company borrowed the Term Loan B tranche of $16.5 million. The Company's ability to draw an additional $16.5 million under Term Loan C was subject to the satisfaction of one or more specified triggers related to the results of the Company's Phase 2b clinical trial of TRV027, which were announced in May 2016. Although those triggers were not attained, in December 2016, the Company and the lenders modified the terms and conditions under which the Company could exercise an option to draw $10 million of Term Loan C. As modified, the Company may draw $10.0 million of Term Loan C no later than March 31, 2017 and upon the lender's receipt of (a) satisfactory evidence that each of the two Phase 3 efficacy trials of OLINVO (i.e., APOLLO-1 and APOLLO-2) have met their respective primary endpoints and (b) a certificate from the Company concerning the ongoing ATHENA open label safety study of OLINVO. Based on the positive results of the Phase 3 efficacy trials of OLINVO announced in February 2017, the Company believes it is now eligible to draw $10.0 million of Term Loan C under the credit facility until March 31, 2017.

Borrowings under Term Loans A and B accrue interest at a fixed rate of 6.50% per annum. The applicable interest rate for Term Loan C will be the greater of (i) 6.5% and (ii) the sum of (a) 6.0% and (b) the 30-day U.S. LIBOR rate as of the date that is three days prior to the funding date of Term Loan C. The Company is required to make payments of interest only on borrowings under the loan agreement on a monthly basis through and including January 1, 2018, after which payments of principal in equal monthly installments and accrued interest will be due until the loan matures on March 1, 2020. If during the period from October 4, 2016 to March 31, 2017, the Company has received net cash proceeds of at least $50.0 million from the sale of its equity securities or from a joint venture, collaboration or other strategic partnering transaction, the maturity date will be further extended to December 1, 2020.

The Company paid the lenders a facility fee of $0.2 million in connection with the execution of the original agreement and immaterial amendment fees in connection with the execution of the second and third amendments to the agreement. Upon the last payment date of the amounts borrowed under the agreement, the Company will be required to pay a final payment fee equal to 6.6% of the aggregate amounts borrowed. This final payment fee will be further increased to 7.0% if during the period from October 4, 2016 to March 31, 2017, the Company has received net cash proceeds of at least $50.0 million from the sale of the Company's equity securities or from a joint venture, collaboration or other strategic partnering transaction. In addition, if the Company repays Term Loan A and Term Loan B prior to the applicable maturity date, it will pay the Lenders a prepayment fee of 2.0% percent of the total amount prepaid if the prepayment occurs between December 23, 2016 and December 23, 2017, and 1.0% percent of the total amount prepaid if the prepayment occurs on or after December 24, 2017.

The Company's obligations under the loan and security agreement are secured by a first priority security interest in substantially all of the assets of the Company, other than intellectual property. The Company has agreed not to

pledge or otherwise encumber its intellectual property, other than through grants of certain permitted non-exclusive or exclusive licenses or other conveyances of its intellectual property.

The loan and security agreement includes affirmative and restrictive covenants, including: (a) financial reporting requirements; (b) limitations on the incurrence of indebtedness; (c) limitations on liens; (d) limitations on certain merger and acquisition transactions; (e) limitations on dispositions of certain assets; (f) limitations on fundamental corporate changes (including changes in control); (g) limitations on investments; (h) limitations on payments and distributions and (i) other covenants. The agreement also contains certain events of default, including for payment defaults, breaches of covenants, a material adverse change in the collateral, the Company's business, operations or condition (financial or otherwise), certain levies, attachments and other restraints on the Company's business, insolvency, defaults under other agreements and misrepresentations.

Three Point Capital, LLC served as a placement agent in connection with the term loans. The Company paid the agent $0.1 million upon execution of the agreement and $0.1 million upon its draw of Term Loan B.

In connection with entering into the agreement, the Company issued to the lenders and the placement agent warrants to purchase an aggregate of 7,678 shares of Trevena common stock; warrants to purchase an aggregate of 5,728 shares remain outstanding as of December 31, 2016. These detachable warrant instruments have qualified for equity classification and have been allocated upon the relative fair value of the base instrument and the warrants, according to the guidance of ASC 470-20-25-2. These warrants are exercisable immediately and have an exercise price of $5.8610 per share. The warrants may be exercised on a cashless basis and will terminate on the earlier of September 19, 2024 or the closing of a merger or consolidation transaction in which the Company is not the surviving entity. In connection with the draw of Term Loan B, the Company issued to the lenders and the placement agent additional warrants to purchase an aggregate of 34,961 shares of Trevena common stock. These warrants have substantially the same terms as those noted above, have an exercise price of $10.6190 per share and an expiration date of December 23, 2025.

As of December 31, 2016, borrowings of $18.5 million attributable to Term Loans A and B are outstanding. Interest expense of $1.2 million and $0.2 million was recorded during the years ended December 31, 2016 and 2015, respectively, with immaterial amounts recorded in 2014. The Company incurred lender and third party costs of $0.2 million and $0.1 million, respectively, related to the issuance of Term Loan A. The Company incurred immaterial lender and third party costs related to the issuance of Term Loan B. The lender costs are classified as a debt discount and the third party costs are classified as debt issuance costs. Per ASU 2015-03, *Interest-Imputation of Interest*, debt discount and debt issuance costs are to be presented as a contra-liability to the debt on the balance sheet. These costs will be amortized to interest expense over the life of the loans using the effective interest method. A total of $0.1 million and $0.1 millions of debt discount and debt issuance costs was amortized to interest expense during the years ended December 31, 2016 and 2015, respectively, with immaterial amounts recorded in 2014.

The following table summarizes how the issuance of Term Loans A and B are reflected on the balance sheet at December 31, 2016 (in thousands):

	December 31, 2016
Gross proceeds	$ 18,500
Debt discount and debt issuance costs	(191)
Carrying value	18,309
Current portion of loans payable, net	5,039
Loans payable, net	$ 13,270

Aggregate maturities of long term debt as of December 31, 2016 are as follows (in thousands):

2017	$ 5,139
2018	6,167
2019	6,167
2020	1,027
2021	—
	$ 18,500
Debt Discount and deferred financing costs	(191)
	$ 18,309

7. Stockholders' Equity

Equity Offerings

Under its certificate of incorporation, the Company was authorized to issue up to 100,000,000 shares of common stock as of December 31, 2016 and December 31, 2015, respectively. The Company also was authorized to issue up to 5,000,000 shares of preferred stock as of December 31, 2016. The Company is required, at all times, to reserve and keep available out of its authorized but unissued shares of common stock sufficient shares to effect the conversion of the shares of the preferred stock and all outstanding stock options and warrants.

On December 14, 2015, the Company entered into an at the market, or ATM, sales agreement with Cowen and Company, LLC, or Cowen, to offer and sell, from time to time at its sole discretion, shares of its common stock, par value $0.001 per share, having an aggregate offering price of up to $75.0 million through Cowen as its sales agent. Sales of the shares are deemed to be "at the market offerings", as defined in Rule 415 under the Securities Act of 1933, as amended. The Company will pay Cowen a commission of up to three percent of the gross sales proceeds and provided Cowen with customary indemnification rights. In 2016, the Company issued and sold 4,815,491 shares of common stock under this ATM facility at a weighted average price per share of $6.865 resulting in gross proceeds of $33.1 million. The net offering proceeds to the Company were approximately $32.1 million after deducting related expenses, including commissions. See Note 15.

On September 16, 2015, the Company issued and sold 7,475,000 shares of common stock in a public offering at a price of $9.75 per share, for gross proceeds of approximately $72.9 million. The net offering proceeds to the Company were approximately $68.3 million, after deducting underwriting discounts and commissions of approximately $4.4 million and offering costs of $0.2 million.

On April 3, 2015, the Company entered into an ATM agreement with Cowen to offer and sell, from time to time at the Company's sole discretion, shares of its common stock, par value $0.001 per share, having an aggregate offering price of up to $40.0 million through Cowen as its sales agent. The Company paid Cowen a commission of up to three percent of the gross sales proceeds and provided Cowen with customary indemnification rights. In 2015, the Company issued and sold an aggregate of 3,700,000 shares of common stock at a weighted average price per share of $6.0001 for aggregate gross proceeds of $22.9 million. The net offering proceeds to the Company were approximately $22.0 million after deducting related expenses, including commissions. This ATM agreement is no longer in effect.

On December 10, 2014, the Company issued and sold 11,250,000 shares of common stock in a public offering of shares as well as 1,598,000 shares of common stock pursuant to the partial exercise of the underwriters' over-allotment option for a total of 12,848,000 shares at a price of $4.00 per share, for aggregate gross proceeds of approximately $51.4 million.

On February 5, 2014, the Company issued and sold 9,250,000 shares of common stock in an IPO at a price of $7.00 per share, for aggregate gross proceeds of approximately $64.8 million. On March 6, 2014, in connection with the partial exercise of the IPO underwriters' over-allotment option, the Company sold an additional 270,449 shares of common stock at a price of $7.00 per share, for aggregate gross proceeds of approximately $1.9 million.

Equity Incentive Plans

In 2008, the Company adopted the 2008 Equity Incentive Plan, as amended on February 29, 2008, January 7, 2010, July 8, 2010, December 10, 2010, June 23, 2011 and June 17, 2013, collectively, the 2008 Plan, that authorized the Company to grant restricted stock and stock options to eligible employees, directors and consultants to the Company.

In 2013, the Company adopted the 2013 Equity Incentive Plan, as amended on May 14, 2014, collectively, 2013 Plan. The 2013 Plan became effective upon the Company's entry into the underwriting agreement related to its IPO in January 2014 and, as of such date, no further grants were permitted under the 2008 Plan. The 2013 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards and other forms of equity compensation (collectively, stock awards), all of which may be granted to employees, including officers, non-employee directors and consultants of the Company. Additionally, the 2013 Plan provides for the grant of cash and stock based performance awards. The 2013 Plan contains an "evergreen" provision, pursuant to which the number of shares of common stock available for issuance under the plan automatically increases on January 1 of each year beginning in 2015.

On December 15, 2016, the Company adopted the Trevena, Inc. Inducement Plan, or the Inducement Plan, to be effective on January 1, 2017, pursuant to which the Company reserved 500,000 shares of the Company's common stock for issuance under the Inducement Plan. The Plan provides for nonstatutory stock options and restricted stock unit awards. The only persons eligible to receive grants of awards under the Inducement Plan are individuals who satisfy the standards for inducement grants under Nasdaq Marketplace Rule 5635(c)(4) and the related guidance under Nasdaq IM 5635-1, including individuals who were not previously an employee or director of the Company or are following a bona fide period of non-employment, in each case as an inducement material to such individual's agreement to enter into employment with the Company.

Under all Plans, the amount, terms of grants and exercisability provisions are determined by the board of directors or its designee. The term of the options may be up to 10 years, and options are 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 estimated grant-date fair value of the Company's share-based awards is amortized ratably over the awards' service periods. Share-based compensation expense recognized was as follows (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Research and development	$ 3,511	$ 1,460	$ 1,129
General and administrative	2,392	1,967	1,254
Total stock-based compensation	$ 5,903	$ 3,427	$ 2,383

A summary of stock option activity and related information through December 31, 2016 follows:

	Options Outstanding		
	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)
Balance, December 31, 2014	3,574,450	$ 3.75	8.06
Granted	1,645,960	7.16	
Exercised	(384,033)	2.36	
Forfeitures	(206,304)	6.04	
Balance, December 31, 2015	4,630,073	$ 4.98	7.87
Granted	2,067,500	8.43	
Exercised	(149,622)	1.71	
Forfeited/Cancelled	(177,373)	(7.47)	
Balance, December 31, 2016	6,370,578	$ 6.10	7.60
Vested or expected to vest at December 31, 2016	6,370,578	$ 6.10	7.60
Exercisable at December 31, 2016	2,822,838	$ 4.15	6.26

The intrinsic value of the options exercisable as of December 31, 2016 was $6.5 million, based on the Company's closing stock price of $5.88 per share and a weighted average exercise price of $4.15 per share.

The Company uses the Black-Scholes option-pricing model to estimate the fair value of stock options at the grant date. The Black-Scholes model requires the Company to make certain estimates and assumptions, including estimating the fair value of the Company's common stock, assumptions related to the expected price volatility of the Company's stock, the period during which the options will be outstanding, the rate of return on risk-free investments and the expected dividend yield for the Company's stock.

The per-share weighted-average grant date fair value of the options granted to employees and directors during the year ended December 31, 2016, 2015 and 2014 was estimated at $5.26, $4.49 and $4.43 per share, respectively, on the date of grant using the Black-Scholes option-pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2016	2015	2014
Expected term of options (in years)	6.2	6.2	5.8
Risk-free interest rate	1.5 %	1.7 %	1.8 %
Expected volatility	68.6 %	68.5 %	75.9 %
Dividend yield	0 %	0 %	0 %

The weighted-average valuation assumptions were determined as follows:

- Risk-free interest rate: The Company based the risk-free interest rate 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 option term.

- Expected term of options: Due to its lack of sufficient historical data, the Company estimates the expected life of its employee stock options using the "simplified" method, as prescribed in Staff Accounting Bulletin No. 107, whereby the expected life equals the arithmetic average of the vesting term and the original contractual term of the option.

- Expected stock price volatility: The Company estimated the expected volatility based on actual historical volatility of the stock price of similar companies with publicly-traded equity securities. The Company calculated the historical volatility of the selected companies by using daily closing prices over a period of the expected term of the associated award. The companies were selected based on their enterprise value, risk profiles, position within the industry and with historical share price information sufficient to meet the expected term of the associated award. A decrease in the selected volatility would have decreased the fair value of the underlying instrument.

- Expected annual dividend yield: The Company estimated the expected dividend yield based on consideration of its historical dividend experience and future dividend expectations. The Company has not historically declared or paid dividends to stockholders. Moreover, it does not intend to pay dividends in the future, but instead expects to retain any earnings to invest in the continued growth of the business. Accordingly, the Company assumed an expected dividend yield of 0.0%.

- Estimated forfeiture rate: In 2016, the Company adopted ASU 2016-09 and will no longer utilize an estimated forfeiture rate. The Company will record forfeitures upon occurrence. The Company's historically estimated annual forfeiture rate on 2015 and 2014 stock option grants was 9% and 7%, respectively, based on the historical forfeiture experience.

The fair value of the Company's common stock, prior to the IPO, was determined by its board of directors with assistance from its management. The board of directors and management considered numerous objective and subjective factors in the assessment of fair value, including the price for the Company's preferred stock that was sold to investors and the rights, preferences and privileges of the preferred stock and common stock, the Company's financial condition and results of operations during the relevant periods and the status of strategic initiatives. These estimates involved a significant level of judgment.

As of December 31, 2016, there was $13.6 million of total unrecognized compensation expense related to unvested options that will be recognized over the weighted average remaining period of 2.69 years.

Shares Available for Future Grant

At December 31, 2016, the Company has the following shares available to be granted under the 2013 Plan:

Available at December 31, 2015	959,354
Authorized	2,032,104
Granted	(2,067,500)
Forfeited/Cancelled	177,373
Available at December 31, 2016	1,101,331

Shares Reserved for Future Issuance

At December 31, 2016, the Company has reserved the following shares of common stock for issuance:

Stock options outstanding	6,370,578
Shares available for future grant under 2013 Plan	1,101,331
Employee stock purchase plan	225,806
Warrants outstanding	60,850
Total shares of common stock reserved for future issuance	7,758,565

8. Commitments and Contingencies

Licenses

On May 3, 2013, the Company entered into an agreement with Allergan plc (formerly Actavis plc and Forest Laboratories Holdings Limited) ("Allergan"), under which the Company granted to Allergan an exclusive option to license its product candidate, TRV027.

Under the option agreement, the Company conducted, at its expense, a Phase 2b trial of TRV027 in acute heart failure. In March 2015, Allergan and the Company signed a letter agreement pursuant to which Allergan paid the Company $10.0 million to fund the expansion of the Phase 2b trial of TRV027 from 500 patients to 620 patients. Collaboration revenue was recognized on a straight-line basis over the study period and was fully recognized as of June 30, 2016. The March 2015 letter agreement does not otherwise amend the terms of the May 2013 option agreement.

In August 2016, Allergan notified the Company of its decision not to exercise its option. As such, the Company has retained all rights to TRV027.

Operating Leases

The Company leases office and laboratory space in Pennsylvania. The Company's leases contain escalating rent clauses, which require higher rent payments in future years. The Company expenses rent on a straight-line basis over the term of the lease, including any rent-free periods. In July 2013, the Company extended the lease for the Company's office and laboratory lease in King of Prussia Pennsylvania until September 2020. In 2014 and 2015, the Company extended the square footage of the lease. The Company has the option to terminate the lease after May 31, 2018 with a required termination payment of $150,000. In addition, the Company leases vivarium space in Pennsylvania. The vivarium lease can be terminated at any time upon 90 days' written notice by the Company.

In December 2016, we entered into a 130-month office lease for approximately 40,565 square feet of space in Wayne, Pennsylvania for the Company's new principal executive office; the term for this lease is expected to commence in the third quarter of 2017. This lease also contains an exclusive option, exercisable until April 1, 2017, to lease up to an additional approximately 13,055 square feet of space at this location.

Rent expense under operating leases was $0.6 million, $0.6 million and $0.5 million in 2016, 2015 and 2014, respectively.

Future minimum lease payments, including termination fees, under noncancelable lease agreements as of December 31, 2016, are as follows (in thousands):

	Operating Lease
2017	$ 404
2018	951
2019	1,436
2020	1,379
2021 and beyond	8,874
Total minimum lease payments	$ 13,044

The Company had deferred rent of $0.2 million and $0.3 million at December 31, 2016 and 2015, respectively. This balance related entirely to the King of Prussia, Pennsylvania lease.

Legal Proceedings

The Company is not involved in any legal proceeding that it expects to have a material effect on its business, financial condition, results of operations and cash flows.

9. Revenue

For arrangements with multiple elements, the Company recognizes revenue in accordance with the FASB's Accounting Standards Update No. 2009-13, Multiple-Deliverable Revenue Arrangements, which provides guidance for separating and allocating consideration in a multiple element arrangement. Deliverables under the arrangement are separate units of accounting if the delivered item has value to the customer on a standalone basis and if the arrangement includes a general right of return relative to the delivery or performance of the undelivered item is considered probable and substantially within the Company's control. The consideration that is fixed or determinable at the inception of the arrangement is allocated to the separate units of accounting based on their relative selling prices. Management exercises significant judgement in determining whether a deliverable is a separate unit of accounting.

In determining the separate units of accounting, the Company evaluates whether the components have standalone value to the collaborator based on consideration of the relevant facts and circumstances for each arrangements. Whenever the Company determines that an element is delivered over a period of time, revenue is recognized using either a proportional performance model, if a pattern of performance can be determined, or a straight-line model over the period of performance, which is typically the research and development term.

The Company entered into a letter agreement with Allergan in March 2015 under which the Company received a nonrefundable upfront fee of $10.0 million. The terms of this agreement contained multiple deliverables which included (i) research and development activities and (ii) testing and analysis related to the ongoing Phase 2b trial of TRV027. Collaboration revenue is recognized only when the price is fixed or determinable, persuasive evidence of an arrangement exists, delivery has occurred or the services have been rendered and the Company has fulfilled its performance obligations under the contract. The Allergan collaboration revenue was recorded on a straight-line basis and was fully recognized as of June 30, 2016. For the years ended December 31, 2016 and 2015, the Company recognized collaboration revenue of $3.8 million and $6.2 million, respectively, related to this agreement.

10. Net Loss Per Common Share

The following table sets forth the computation of basic and diluted net loss per share for the periods indicated (in thousands, except share and per share data):

	Year Ended December 31,		
	2016	2015	2014
Basic and diluted net loss per common share calculation:			
Net loss	$ (102,994)	$ (50,528)	$ (49,701)
Accretion of redeemable convertible preferred stock	—	—	(29)
Net loss attributable to common stockholders	$ (102,994)	$ (50,528)	$ (49,730)
Weighted average common shares outstanding	52,398,521	43,794,276	24,655,603
Net loss per share of common stock - basic and diluted	$ (1.97)	$ (1.15)	$ (2.02)

The following outstanding securities at December, 31, 2016, 2015 and 2014 have been excluded from the computation of diluted weighted shares outstanding, as they would have been anti-dilutive:

	December 31,		
	2016	2015	2014
Options outstanding	6,370,578	4,630,073	3,574,450
Warrants	60,850	62,800	30,258
Total	6,431,428	4,692,873	3,604,708

11. Comprehensive Income (Loss)

The following table presents changes in the components of accumulated other comprehensive income or loss, net of tax (in thousands):

Balance, January 1, 2015	$ (19)
Net unrealized loss arising during the period	(187)
Balance, December 31, 2015	$ (206)
Net unrealized gains on marketable securities	208
Balance, December 31, 2016	$ 2

There were no reclassifications out of accumulated other comprehensive income or loss as well as no tax effect for all periods presented.

12. Income Taxes

As the Company has historically incurred net operating losses, the Company has not recorded a provision for income taxes.

Deferred tax assets and liabilities reflect the net effects of net operating loss and tax credit carryovers and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company maintains a full valuation allowance against its net deferred tax assets because significant utilization of such amounts is not presently expected in the foreseeable future.

Significant components of the Company’s net deferred tax assets as of December 31 are as follows (in thousands):

	December 31,	
	2016	2015
Deferred tax assets:		
Net operating loss carryforwards	$ 15,748	$ 11,649
Research and development credits	11,020	6,825
Research and development expenses capitalized for tax purposes	97,495	61,074
Deferred rent	97	104
Depreciation	553	552
Other temporary differences	1,895	653
Total deferred tax assets	126,808	80,857
Deferred tax liabilities:		
Prepaid expenses	(105)	(82)
Total deferred tax liabilities	(105)	(82)
Net deferred tax assets	126,703	80,775
Less valuation allowance	(126,703)	(80,775)
Net deferred tax asset	$ —	$ —

A reconciliation of income tax expense computed at the statutory federal income tax rate to income taxes as reflected in the financial statements is as follows:

	December 31,		
	2016	2015	2014
Percent of pre-tax income:			
U.S. federal statutory income tax rate	34.0 %	34.0 %	34.0 %
Permanent Differences	0.0 %	0.1 %	(0.6)%
State taxes, net of federal benefit	6.6 %	6.6 %	6.5 %
Research and development credit	4.0 %	3.9 %	3.9 %
Other	0.0 %	0.3 %	0.0 %
Change in valuation allowance	(44.6)%	(44.9)%	(43.8)%
Effective income tax rate	0.0 %	0.0 %	0.0 %

As of December 31, 2016, the Company had federal and state net operating loss carryforwards of $38.8 million that begin to expire at various dates starting in 2027. As of December 31, 2016, the Company had federal research and development tax credit carryforwards of $11.0 million that begin to expire at various dates starting in 2027. The Company's ability to utilize net operating loss carryforwards, or NOLs, or tax credit carryforwards may be subject to annual limitations under certain provisions of the Internal Revenue Code related to "changes in ownership."

The Company files income tax returns in the U.S. and the Commonwealth of Pennsylvania. Tax years for fiscal 2013 through 2016 are open and potentially subject to examination by the federal and state taxing authorities. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years. To the extent the Company utilizes in the future any tax attribute NOL carryforwards from a tax period that may otherwise be closed to examination, the Internal Revenue Service, state tax authorities, or other governing parties may still adjust the NOL carryforwards upon their examination of the future period in which the attribute was utilized.

13. Employee Benefit Plan

The Company sponsors a 401(k) defined contribution plan for its employees. Employee contributions are voluntary. The Company matches employee contributions in an amount equal to 100% of the first 3% of eligible compensation and 50% of the next 2% of eligible compensation, and such employer contributions are immediately vested. During 2016, 2015 and 2014, the Company provided matching contributions of $0.4 million, $0.3 million and $0.2 million, respectively.

14. Selected Quarterly Financial Data (Unaudited)

	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
	(in thousands, except share and per share amounts)			
2016				
Total revenue	$ 1,875	$ 1,875	$ —	$ —
Loss from operations	(17,749)	(19,104)	(29,713)	(35,717)
Net loss	$ (17,732)	$ (19,295)	$ (29,985)	$ (35,982)
Net loss per share of common, basic and diluted	$ (0.35)	$ (0.37)	$ (0.57)	$ (0.67)
Weighted average shares outstanding, basic and diluted	51,350,365	52,174,569	52,205,156	53,850,166
2015				
Total revenue	$ 625	$ 1,875	$ 1,875	$ 1,875
Loss from operations	(13,064)	(11,508)	(10,555)	(15,494)
Net loss	$ (12,930)	$ (11,519)	$ (10,615)	$ (15,464)
Net loss per share of common, basic and diluted	$ (0.33)	$ (0.44)	$ (0.24)	$ (0.30)
Weighted average shares outstanding, basic and diluted	39,251,184	40,809,931	44,214,428	50,770,359

The quarters presented above for 2016 have been adjusted to reflect the adoption of ASU 2016-09 and related impact, that is deemed immaterial, of electing to recognize forfeitures of share-based payment awards as they occur rather than using an estimate.

15. Subsequent Events

Equity Offerings

In January 2017, the Company issued and sold 1,081,550 shares of common stock through Cowen, pursuant to the December 2015 ATM sales. The shares were sold at a weighted average price per share of $6.50. The net offering proceeds to the Company were approximately $6.8 million after deducting related expenses, including commissions. Approximately $34.9 million remained available under the ATM sales facility as of March 1, 2017.

Loans Payable

On February 21, 2017, we announced positive top-line results from our Phase 3 APOLLO-1 and APOLLO-2 pivotal efficacy studies of OLINVO in moderate-to-severe acute pain following bunionectomy and abdominoplasty, respectively. In both studies, all dose regimens achieved their primary endpoint of statistically greater analgesic efficacy than placebo, as measured by responder rate. Based on these results, the Company believes it is now eligible to draw $10.0 million of Term Loan C under our loan and security agreement with Oxford Finance LLC and Pacific Western Bank, as discussed in Note 6. In addition, monthly interest only payments have been extended to January 1, 2018.

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

An evaluation was performed under the supervision and with the participation of our management, including our Chief Executive Officer, or CEO, and our Chief Financial Officer, or CFO, of the effectiveness of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) promulgated under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as of December 31, 2016.

Based on that evaluation, our management, including our CEO and CFO, concluded that as of December 31, 2016 our disclosure controls and procedures were effective to ensure that information required to be disclosed by us in reports that we file or submit under the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission and that such information is accumulated and communicated to the Company's management, including our CEO and CFO, as appropriate to allow timely decisions regarding required disclosure.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting and Attestation Report of the Registered Public Accounting Firm

Management's Report on Internal Control Over Financial Reporting is included in Part II, Item 8 of this Annual Report on Form 10-K and incorporated into this Item 9A by reference.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting as required by Section 404(c) of the Sarbanes Oxley Act of 2002. Because the Company qualifies as an emerging growth company under the JOBS Act, management's report was not subject to attestation by our registered public accounting firm.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Directors

The information required by this Item 10 with respect to our Directors is incorporated herein by reference to the information contained under the caption "Item 1. Election of Directors" in our definitive proxy statement related to the 2017 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

Executive Officers

The information concerning our executive offers required by this Item 10 is provided under the caption "Executive Officers" in Part I, Item 1 of this Annual Report on Form 10-K.

Section 16(a) Beneficial Ownership Reporting Compliance

The information concerning Section 16(a) Beneficial Ownership Reporting Compliance by our directors and executive officers is incorporated by reference to the information contained under the caption "Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive proxy statement related to the 2017 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

Code of Ethics

The information concerning our Code of Business Conduct and Ethics is incorporated by reference to the information contained under the caption "Code of Ethics" in our definitive proxy statement related to the 2017 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

Audit Committee

The information required by this Item 10 with respect to our Audit Committee is incorporated herein by reference to the information contained under the caption "Corporate Governance" in our definitive proxy statement related to the 2017 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 is incorporated by reference to the information contained in our definitive proxy statement related to the 2017 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by Item 12 is incorporated by reference to the information contained in our definitive proxy statement related to the 2016 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

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

The information required by Item 13 is incorporated by reference to the information contained in our definitive proxy statement related to the 2017 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by Item 14 is incorporated by reference to the information contained in our definitive proxy statement related to the 2017 annual meeting of stockholders, to be filed within 120 days after the end of the year covered by this Annual Report on Form 10-K.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) DOCUMENTS FILED AS PART OF THIS REPORT

The following is a list of our financial statements and supplementary data included in this Annual Report on Form 10-K under Item 8 of Part II hereof:

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Notes to Financial Statements for the years ended December 31, 2016, 2015 and 2014.	77

(b) EXHIBITS

The following is a list of exhibits filed as part of this Annual Report on Form 10-K. Where so indicated by footnote, exhibits that were previously filed are incorporated by reference. For exhibits incorporated by reference, the location of the exhibit in the previous filing is indicated.

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on February 5, 2014).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed with the SEC on February 5, 2014).
4.1	Reference is made to Exhibits 3.1 and 3.2.
4.2	Specimen stock certificate evidencing shares of Common Stock of the Registrant (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
4.3	Form Warrant issued by Trevena, Inc. to Oxford Finance LLC, Pacific Western Bank and Three Point Capital, LLC (incorporated by reference to Exhibit 4.1 to Registrant's Current Report on Form 8-K, filed with the SEC on December 23, 2015).
10.1*	License Agreement, dated as of May 3, 2013, by and between the Registrant and Forest Laboratories Holdings Limited (now Allergan plc) (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.2*	Option Agreement, dated as of May 3, 2013, by and between the Registrant and Forest Laboratories Holdings Limited (now Allergan plc) (incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.3	Letter Agreement dated March 5, 2015 between Trevena, Inc. and Actavis plc (now Allergan plc) (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on March 10, 2015).
10.4	Warrant to purchase shares of Series B preferred stock issued to Comerica Bank, dated December 9, 2011 (incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.5	Warrant to purchase shares of Common Stock issued to Silicon Valley Bank, dated June 24, 2008 (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.6	Amended and Restated Investor Rights Agreement, dated as of May 3, 2013, by and among the Registrant and certain of its stockholders (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.7	Commercial Lease Agreement, dated as of August 4, 2008, by and between the Registrant and Pios Grande KOP Business Center, L.P. (successor-in-interest to KOPBC, Inc.) (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.8	Amendment No. 1 to Commercial Lease Agreement, dated as of December 8, 2008, by and between the Registrant and Pios Grande KOP Business Center, L.P. (successor-in-interest to KOPBC, Inc.) (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).

10.9	Amendment No. 2 to Commercial Lease Agreement, dated as of July 3, 2013, by and between the Registrant and Pios Grande KOP Business Center, L.P. (successor-in-interest to KOPBC, Inc.) (incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.10	Third Amendment to Commercial Lease Agreement, dated as of February 21, 2014, by and between the Registrant and Pios Grande KOP Business Center, L.P. (successor-in-interest to KOPBC, Inc.) (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-200386), originally filed with the SEC on November 20, 2014).
10.11	4th Amendment to Commercial Lease Agreement dated as of January 30, 2015, by and between the Registrant and Pios Grande KOP Business Center, L.P. (successor-in-interest KOPBC, Inc.) (incorporated by reference to Exhibit 10.4 to Registrant's Quarterly Report on Form 10-Q, filed with the SEC on May 7, 2015).
10.12#	Agreement of Lease between Chesterbrook Partners, LP and Trevena, Inc. for 955 Chesterbrook Blvd., Suite 200, Wayne, PA, dated as of December 9, 2016.
10.13+	2008 Equity Incentive Plan, as amended to date (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S 1, as amended (File No. 333 191643), originally filed with the SEC on October 9, 2013).
10.14+	Form of Stock Option Agreement under 2008 Equity Incentive Plan (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.15+	2013 Equity Incentive Plan (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.16+	Form of Stock Option Grant Notice and Stock Option Agreement under 2013 Equity Incentive Plan (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.17+	Form of Stock Option Grant Notice and Stock Option Agreement under 2013 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 to Registrant's Quarterly Report on Form 10-Q, filed with the SEC on May 7, 2015).
10.18+	Form of Restricted Stock Grant Notice and Restricted Stock Unit Award Agreement under 2013 Equity Incentive Plan (incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.19+	Trevena, Inc. Inducement Plan, effective January 1, 2017 (incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K, filed with the SEC on December 19, 2016).
10.20+	Form of Stock Option Grant Notice and Stock Option Agreement used in connection with the Trevena, Inc. Inducement Plan (incorporated by referenced to Exhibit 10.2 to Registrant's Current Report on Form 8-K, filed with the SEC on December 19, 2016).
10.21+	Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Award Agreement used in connection with Trevena, Inc. Inducement Plan (incorporated by reference to Exhibit 10.3 to Registrant's Current Report on Form 8-K, filed with the SEC on December 19, 2016).
10.22+	Trevena, Inc. Incentive Compensation Plan, effective as of January 1, 2015 (incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K, filed with the SEC on January 5, 2015).
10.23+	Non-Employee Director Compensation Plan (incorporated by reference to Exhibit 10.14 to the Registrant's Current Report on Form 8-K filed with the SEC on July 1, 2014).
10.24+	Trevena, Inc. Non-Employee Director Compensation Policy, effective as of January 1, 2016 (incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K, filed with the SEC on December 11, 2015).

10.25+	2013 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.26+	Form of Indemnity Agreement with executives and directors (incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-191643), originally filed with the SEC on October 9, 2013).
10.27+	Employment Agreement, dated as of January 31, 2014, by and between the Registrant and Maxine Gowen (incorporated by reference to Exhibit 10.17 to the Registrant's Form 10-K filed with the SEC on March 20, 2014).
10.28+	Amendment to Executive Employment Agreement dated as of May 14, 2015 by and between Trevena, Inc. and Maxine Gowen, Ph.D. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, originally filed with the SEC on May 5, 2015).
10.29+	Second Amendment to Executive Employment Agreement dated as of January 6, 2017 by and between Trevena, Inc. and Maxine Gowen, Ph.D. (incorporated by referenced to Exhibit 10.1 to Registrant's Current Report on Form 8-K, filed with the SEC on January 6, 2017).
10.30+	Employment Agreement, dated as of January 31, 2014, by and between the Registrant and Michael Lark (incorporated by reference to Exhibit 10.18 to the Registrant's Form 10-K filed with the SEC on March 20, 2014).
10.31+	Employment Agreement, dated as of January 31, 2014, by and between the Registrant and Roberto Cuca (incorporated by reference to Exhibit 10.19 to the Registrant's Form 10-K filed with the SEC on March 20, 2014).
10.32+	Employment Agreement, dated as of January 31, 2014, by and between the Registrant and David Soergel (incorporated by reference to Exhibit 10.20 to the Registrant's Form 10-K filed with the SEC on March 20, 2014).
10.33+	Employment Agreement dated as of May 12, 2014, by and between the Registrant and John M. Limongelli (incorporated by reference to Exhibit 10.1 to the Registrant's Form 8-K filed with the SEC on May 15, 2014).
10.34+	Omnibus Amendment to Employment Agreements dated as of May 4, 2015 by and between Trevena, Inc. and each of Roberto Cuca, Michael Lark, John M. Limongelli and David Soergel (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, filed with the SEC on May 5, 2015).
10.35+	Omnibus Amendment to Employment Agreements dated January 6, 2017 by and between Trevena, Inc. and each of Carrie L. Bourdow, Roberto Cuca, Yacoub Habib, Michael Lark, John M. Limongelli and David Soergel (incorporated by reference to Exhibit 10.2 to Registrant's Current Report on Form 8-K, filed with the SEC on January 6, 2017).
10.36+	Executive Employment Agreement effective as of May 4, 2015 by Trevena, Inc. and Carrie L. Bourdow (incorporated by reference to Exhibit 10.3 to Registrant's Current Report on Form 8-K, originally filed with the SEC on May 5, 2015).
10.37+	Executive Employment Agreement effective as of July 20, 2015 by and between Trevena, Inc. and Yacoub Habib (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, originally filed with the SEC on July 21, 2015).
10.38+	First Amendment to Executive Employment Agreement effective as of January 1, 2016 by and between Trevena, Inc. and Yacoub Habib (incorporated by reference to Exhibit 10.1 to the Registrant's Form 10-K filed with the SEC on March 9, 2016).
10.39	Loan and Security Agreement, dated September 19, 2014, by and among Trevena, Inc., as borrower, Oxford Finance LLC, as collateral agent and lender, and Square 1 Bank, as lender (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on September 22, 2014).

10.40	First Amendment to Loan and Security Agreement, dated April 13, 2015, by and among Trevena, Inc., as borrower, Oxford Finance LLC, as collateral agent and lender, and Square 1 Bank, as lender (incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K, filed with the SEC on April 13, 2015).
10.41	Second Amendment to Loan and Security Agreement dated December 23, 2015, by and among Trevena, Inc., as borrower, Oxford Finance LLC, as collateral agent and lender, and Pacific Western Bank (as the successor to Square 1 Bank), as lender (incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K, filed with the SEC on December 23, 2015).
10.42	Third Amendment to Loan and Security Agreement dated December 30, 2016, by and between Trevena, Inc., as borrower, Oxford Finance LLC, as collateral agent and lender, and Pacific Western Bank (as successor to Square 1 Bank), as lender (incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K, filed with the SEC on January 4, 2017).
10.43	Common Stock Sales Agreement, dated December 14, 2015, by and between Trevena, Inc. and Cowen and Company, LLC (incorporated by reference to Exhibit 10.1 to Registrant's Current Report on Form 8-K, filed with the SEC on December 14, 2015).
12.1#	Statement Regarding Computation of Ratios.
23.1#	Consent of Independent Registered Public Accounting Firm.
24.1#	Power of Attorney. Reference is made to the signature page hereto.
31.1#	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
31.2#	Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1#	Certification of the Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2#	Certification of the Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101#	The following financial information from this Annual Report on Form 10-K for the periods ended December 31, 2016 and 2015, formatted in XBRL (eXtensible Business Reporting Language): (i) Balance Sheets as of December 31, 2016 and 2015, (ii) Statements of Operations and Comprehensive Loss for the years ended December 31, 2016, 2015 and 2014, (iii) Statement of Redeemable Convertible Preferred Stock and Stockholders' Equity as of December 31, 2016, 2015 and 2014, (iv) Statements of Cash Flows for the years ended December 31, 2016, 2015 and 2014 and (v) Notes to Financial Statements, tagged as blocks of text.

Filed herewith.

\+ Indicates management contract or compensatory plan.

* Portions of this exhibit, indicated by asterisks, have been omitted and separately filed with the Securities and Exchange Commission pursuant to a request for confidential treatment that has been granted by the Securities and Exchange Commission.

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.

Date: March 8, 2017

TREVENA, INC.
By: /s/ Maxine Gowen

Maxine Gowen
President and Chief Executive Officer

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

Signature	Title	Date
/s/ Maxine Gowen Maxine Gowen	President and Chief Executive Officer (Principal Executive Officer) and Director	March 8, 2017
/s/ Roberto Cuca Roberto Cuca	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 8, 2017
/s/ Leon O. Moulder, Jr. Leon O. Moulder, Jr	Chairman, Board of Directors	March 8, 2017
/s/ Michael R. Dougherty Michael R. Dougherty	Director	March 8, 2017
/s/ Adam M. Koppel Adam M. Koppel, M.D., Ph.D.	Director	March 8, 2017
/s/ Julie H. McHugh Julie H. McHugh	Director	March 8, 2017
/s/ Jake R. Nunn Jake R. Nunn	Director	March 8, 2017
/s/ Anne M. Phillips Anne M. Phillips, M.D.	Director	March 8, 2017
/s/ Barbara Yanni Barbara Yanni	Director	March 8, 2017

EXHIBIT INDEX

Exhibit Number	Description
10.12	Agreement of Lease between Chesterbrook Partners, LP and Trevena, Inc. for 955 Chesterbrook Blvd., Suite 200, Wayne, PA, dated as of December 9, 2016.
12.1	Statement Regarding Computation of Ratios.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney. Reference is made to the signature page hereto.
31.1	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1	Certification of the Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of the Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following financial information from this Annual Report on Form 10-K for the periods ended December 31, 2016 and 2015, formatted in XBRL (eXtensible Business Reporting Language): (i) Balance Sheets as of December 31, 2016 and 2015, (ii) Statements of Operations and Comprehensive Loss for the years ended December 31, 2016, 2015 and 2014, (iii) Statement of Redeemable Convertible Preferred Stock and Stockholders' Equity as of December 31, 2016, 2015 and 2014, (iv) Statements of Cash Flows for the years ended December 31, 2016, 2015 and 2014 and (v) Notes to Financial Statements, tagged as blocks of text.

Exhibit 10.12

AGREEMENT OF LEASE

BETWEEN

CHESTERBROOK PARTNERS, LP

AND

TREVENA, INC.

SUITE 200

955 CHESTERBROOK BOULEVARD

CHESTERBROOK CORPORATE CENTER®

TREDYFFRIN TOWNSHIP

CHESTER COUNTY

PENNSYLVANIA

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EXHIBITS

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"B" — Description of the Land

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AGREEMENT OF LEASE

1. **Parties.**

This Lease is made as of December 9, 2016, by and between **CHESTERBROOK PARTNERS, LP**, a limited partnership organized and existing under the laws of the State of Delaware, whose address is Suite 120, 955 Chesterbrook Boulevard, Wayne,

PA 19087 (hereafter called "Landlord"), and **TREVENA, INC.**, a corporation organized and existing under the laws of the state of Delaware whose present address is 1018 W. 8th Avenue, King of Prussia, PA 19406 (hereinafter referred to as "Tenant").

It is hereby agreed by and between Landlord and Tenant, intending to be legally bound, for themselves and for their respective heirs, executors, administrators, successors and assigns, in the manner following, it being understood that the Premises are demised under and subject to the following covenants, all of which are also to be regarded as strict legal conditions.

2. **Demise**.

Landlord does hereby lease and demise to Tenant and Tenant does hereby hire and take from Landlord, for the term and subject to the provisions hereof, the premises (the "Premises") shown cross-hatched on the floor plan(s) (the "Floor Plan") attached hereto as **Exhibit "A,"** consisting of approximately 40,565 rentable square feet on the second floor of the building (hereinafter referred to as the "Building") known as 955 Chesterbrook Boulevard, occupying the parcel of land bounded as described on **Exhibit "B"** attached hereto (the "Land"), together with the right, in common with others, to use the common areas of the Property. The Building and Land are sometimes collectively referred to in this Lease as the "Property". As used herein, "common areas" means those portions of the Property that are designated by Landlord for the common use of tenants and others, such as sidewalks, unreserved parking areas, common corridors, elevator foyers, restrooms, vending areas and lobby areas, entrances, freight and passenger elevators, loading docks, public and private fire stairways, lobby areas and other public portions of the Property which enable Tenant to obtain full use and enjoyment and the Property for all customary purposes.

3. **Term**.

(a) This demise shall be for the term (hereinafter referred to as the "Term") beginning on the "Commencement Date" of the Term as defined in Article 3(b) of this Lease and ending, without the necessity of notice from either party to the other, one hundred thirty (130) months from and after the Commencement Date if the Commencement Date shall be the first day of a month, if the Commencement Date shall be other than the first day of the month, then from and after the first day of the month next following the Commencement Date.

(b) The Commencement Date shall occur on the earlier of:

(i) Substantial Completion of the Tenant Improvements (as defined below), which date is anticipated by the parties to be July 1, 2017, or

(ii) the date Tenant or anyone claiming under or through Tenant first occupies any part of the Premises for business purposes (provided that Tenant accessing the Premises in accordance with this Lease in order to prepare the Premises for Tenant's occupancy (including, without limitation, any move-in and/or fit-out work) shall not constitute occupying the Premises for purposes of this clause).

(c) When the Commencement Date is established, Landlord and Tenant shall promptly execute and acknowledge a memorandum, in the form attached hereto as **Exhibit "C"**, of the Commencement Date and the date of expiration of the Term (the "Expiration Date").

(d) If the Tenant or any person claiming through the Tenant shall have continued to occupy the Premises after the expiration or earlier termination of the Term or any renewal thereof, and if the Landlord shall have consented in writing to such continuation of occupancy, such occupancy (unless the parties hereto shall have otherwise agreed in writing) shall be deemed to be under a month-to-month tenancy. The month-to-month tenancy shall continue until either party shall have notified the other in writing, at least thirty (30) days prior to the end of any calendar month, that the party giving such notice elects to terminate the month-to-month tenancy at the end of that calendar month, in which event, such tenancy shall so terminate. If such occupancy shall have continued without Landlord's written consent, then such occupancy shall be in violation of this Lease, in which event, Tenant (i) shall be liable for any and all losses, claims, costs, expenses and damages actually suffered or incurred by Landlord (including, without limit thereto, court costs and reasonable counsel fees), whether foreseen or unforeseen as a result of such continued occupancy, and Landlord shall have all of the rights and remedies available under this Lease, or at law or in equity, for such violation and, without limitation of the foregoing clause (i), (ii) will indemnify and hold harmless Landlord from and against all claims and demands made by succeeding tenants against Landlord, founded upon delay by Landlord in delivering possession of the Premises to such succeeding tenant, provided that Landlord has given Tenant not less than thirty (30) days' written notice that there is a tenant that will be succeeding to the Premises. The rental payable with respect to each monthly period of any month-to-month tenancy (and to each monthly period of continued occupancy which may occur without Landlord's consent) shall equal one hundred fifty percent (150%) of the Fixed Rent payable under Article 4(b) paid for the immediately preceding lease year. Any month-to-month tenancy arising with Landlord's consent shall be upon the same terms and subject to the same conditions as those which are set forth in this Lease, except as otherwise set forth in this subparagraph (f), provided that if the Landlord shall have given to the Tenant, at least thirty (30) days prior to the expiration or earlier termination of the Term or any renewal thereof or prior to the end of any month of a month-to-month tenancy, written notice that the Tenant's occupancy following such month or expiration or termination (as the case may be) shall be subject to such modifications of the terms and conditions of this Lease (including any provision relating to the amount and payment of rent) as are specified in such notice, the Tenant's occupancy following such month or expiration or termination (as the case may be) shall be subject to the provisions of this Lease as so modified.

4. **Fixed Rent; Tenant Energy Costs; Annual Operating Costs; Taxes**.

(a) Commencing on the Commencement Date, Tenant shall pay to Landlord as rent under this Lease the aggregate of:

(i) Fixed Rent (as defined in Article 4(b) of this Lease);

(ii) Tenant's share of Tenant Energy Costs (as defined in Article 4(d) of this Lease);

(iii) Tenant's proportionate share (as defined in Article 4(c) of this Lease) of increases in Annual Operating Costs (as defined in Article 4(e) of this Lease) over Base Operating Costs (as defined in Article 4(e)(iii) of this Lease);

(iv) Tenant's proportionate share (as defined in Article 4(c) of this Lease) of increases in Annual Tax Costs (as defined in Article 4(f)(i) of this Lease) over Base Tax Costs (as defined in Article 4(f)(ii) of this Lease); and

(v) All other sums payable by Tenant to Landlord pursuant to the provisions of this Lease.

(b) Fixed Rent.

(i) The minimum fixed annual rent (the "Fixed Rent") due each lease year of the Term shall be due and payable in lawful money of the United States of America, in equal monthly installments in advance and without prior demand, notice, set-off or deduction (except as otherwise expressly set forth in this Lease) on the first day of each and every month commencing on the Commencement Date and continuing during the Term in accordance with the following schedule:

Lease Months	$/RSF (40,565)	Annual Fixed Rent	Monthly Fixed Rent
1 — 12*	$26.50	$1,074,972.50	$89,581.04
13 — 24*	$27.00	$1,095,255.00	$91,271.25
25 — 36	$27.50	$1,115,537.50	$92,961.46
37 — 48	$28.00	$1,135,820.00	$94,651.67
49 — 60	$28.50	$1,156,102.50	$96,341.88
61 — 72	$29.00	$1,176,385.00	$98,032.08
73 — 84	$29.50	$1,196,667.50	$99,722.29
85 — 96	$30.00	$1,216,950.00	$101,412.50
97 — 108	$30.50	$1,237,232.50	$103,102.71
109 — 120	$31.00	$1,257,515.00	$104,792.92
121 — 130	$31.50	$1,277,797.50	$106,483.13

* The foregoing notwithstanding, Fixed Rent, but not Tenant Energy Costs, shall be conditionally and completely abated during the following ten (10) full calendar months of the Term: Lease Months 1 — 5; and Lease Months 13 — 17 (the "Rental Abatement Period"). During all other periods of the Term, Tenant shall make Fixed Rent payments without any abatement (except as otherwise expressly provided in this Lease) as provided herein.

Notwithstanding the foregoing, Landlord may, in Landlord's sole discretion, prior to the conclusion of the Rental Abatement Period, elect to provide Tenant with a cash payment equal to any unused Abated Rent. If Landlord makes such election, Landlord shall provide Tenant written notice of such election prior to the conclusion of the Rental Abatement Period. In the event that Landlord elects to pay to Tenant such cash payment, provided Tenant has actually received the entire amount of the cash payment without setoff or deduction, Tenant shall pay the full Fixed Rent as set forth in the above rental chart without any abatement.

(ii) The Fixed Rent and all other sums payable to Landlord pursuant to or by reason of this Lease shall be payable to Landlord as follows:

If payment via check:
Chesterbrook Partners, L.P.
c/o Pitcairn Properties
955 Chesterbrook Boulevard — Suite 120
Chesterbrook, PA 19087

If paying via wire:
Bank of America, N.A.
ABA/Routing No. 026009593
Account Name: Chesterbrook Partners, L.P.
Account No. 0038-3050-5219
SWIFT Code: BOFAUS3N

If paying via ACH:
Bank of America, N.A.
ABA/Routing No. 031202084
Account Name: Chesterbrook Partners, L.P.
Account No. 0038-3050-5219
SWIFT Code: BOFAUS3N

or to such other person and at such other place as Landlord may from time to time designate in writing.

(iii) The first monthly installment of Fixed Rent (applicable to the sixth (6th) full month of the Term) shall be paid at the time of the signing of this Lease. The term "lease year" shall mean each annual period commencing on the Commencement Date and each succeeding anniversary thereof.

(iv) If the Term begins on a day other than the first day of a month, Fixed Rent from the Commencement Date until the first day of the following month shall be prorated and shall be payable in advance on the first day of the Term and, in such event, the installment of Fixed Rent paid at the signing of this Lease shall be applied to the Fixed Rent due for the sixth (6th) full calendar month of the Term.

(c) Tenant's Proportionate Share. As used in this Lease, "the square foot area of the Premises" shall be deemed to be 40,565 square feet, "the total square foot area of the Building" shall be deemed to be 118,235 square feet and "Tenant's proportionate share" shall refer to the percentage relationship between the foregoing, namely 34.31 %, subject to adjustment in accordance with this Lease in the event of a change in the square foot area of the Premises or the total square foot area of the Building. Tenant recognizes that, as used in this Lease, the total square foot area of the Premises includes a share of the common areas of the Building.

(d) Tenant Energy Costs.

(i) The term "Tenant Energy Costs" shall mean the actual costs (without markup but including Landlord's reasonable administrative fee (currently $25.00 per month)) charged by the utility provider to Landlord of furnishing to the respective areas of the Property electric energy or other utility services, except water and sewer (including taxes or fuel adjustment or transfer charges and other like charges regularly passed on to the consumer by the public utility furnishing electric energy to the Property), payable by Tenant pursuant to clause (ii) below, and excluding any overtime charges for other tenants in the Building, and with Landlord having credited any sums paid as direct reimbursement of such costs by other tenants of the Building.

(ii) For and with respect to each calendar year of the Term (and any renewals or extensions thereof) including, without limit, the first calendar year during which the Term of this Lease shall have commenced, there shall accrue, as additional rent under this Lease and be paid within thirty (30) days after Tenant's receipt from Landlord of a statement or statements of the amount due, Landlord's costs in such calendar year of supplying such quantity of electric energy as is; (A) consumed by Tenant in the Premises, including, without limitation, such electric energy as is consumed by Tenant in connection with the operation of the heating, ventilating and air-conditioning systems serving only the Premises, if any, as such consumption shall have been shown on the meters referred to in Article 16(a)(viii) of this Lease, together with any reasonable administrative costs incurred by Landlord by reason thereof, and (B) Tenant's proportionate share, as defined in Article 4(c) of this Lease, of Landlord's costs in such calendar year of supplying electric energy and other utility service (excluding water and sewer), as is supplied to all non-tenanted areas of the Property in connection with the operation of the Property.

(iii) The method and timing (but not more frequently than monthly) of billing such costs of Landlord shall be determined by Landlord, using reasonable accounting principles, it being understood that it is not intended that Landlord derive any profit from the supplying of electric energy or other utility service. At Landlord's option, Landlord may bill Tenant for Tenant's share of Tenant Energy Costs monthly on an estimated basis (which may be adjusted from time to time by Landlord) in advance with a reconciliation of such costs to be made on an annual basis. Tenant shall have the right to audit Tenant Energy Costs on the same basis as Tenant may audit Annual Operating Costs.

(iv) If Tenant shall fail to pay when due any amounts payable by Tenant under this Article 4(d), and such failure shall continue for ten (10) days after Tenant's receipt of written notice from Landlord, then in addition to any other rights and remedies available to Landlord under this Lease, or at law or in equity, Landlord may terminate any utility services to the Premises furnished by Landlord for which payment is overdue, without any liability to Tenant, whether for interruption of Tenant's business or otherwise.

(e) Annual Operating Costs.

(i) The term "Annual Operating Costs" shall mean the actual costs to Landlord of operating and maintaining the Property (including, without limit, all improvements thereto and fixtures and equipment therein or thereon) during each calendar year of the Term

(and any renewals or extensions thereof) including, without limit, the first calendar year during which the Term of this Lease shall have commenced, excluding Tenant Energy Costs and Annual Tax Costs. Such costs shall include, by way of example rather than of limitation, (1) charges or fees for, and taxes on, the furnishing to the Property of water and sewer service, electric energy (excluding the supply of electric energy included in Tenant Energy Costs) and, if the Building systems should be converted to receive the same, steam or fuel and other utility services; (2) costs of elevator service and charges or fees for maintenance of the Property, planting, replanting and janitorial service, trash removal, policing, cleaning, restriping, resurfacing, maintaining and repairing all walkways, roadways, parking areas forming part of the Property, maintaining all landscaped areas of the Property; (3) charges or fees for any necessary governmental permits; (4) wages, salaries and benefits of employees of Landlord who perform duties connected with the operation, maintenance and repair of the Property (to the extent such employees or persons are directly engaged in the repair, operation and maintenance of the Property, are commercially reasonable, and such expenses are not allocated to a leasing agent), management fees (which is a fee separate from the aforementioned expenses for wages, salaries and benefits of employees of Landlord performing duties for the Property, not to exceed five percent (5%) of annual gross rental revenue for the Building), overhead and expenses, provided, that in no event shall Annual Operating Costs for purposes of this Lease include wages, salaries and/or benefits attributable to Building management personnel above the level of the general manager or equivalent; (5) the cost of premiums for hazard, rent, liability, workmen's compensation and other insurance upon the Property or portions thereof; (6) costs arising under service contracts with independent contractors servicing or performing maintenance or other related tasks for the Building; (7) professional and consulting fees including, without limit, legal and auditing fees; (8) repairs, replacements and improvements to the Property which are reasonable and necessary for the continued operation of the Building as a first class office building; and (9) the cost of all other items which, under standard accounting practices, constitute operating or maintenance costs which are attributable to the Property or any portion thereof. Notwithstanding the foregoing, the term "Annual Operating Costs" shall not include: depreciation on the Building or equipment; interest and principal payments on mortgage encumbrances and other debt costs; ground rents; income taxes; salaries of executive officers of Landlord; costs incurred in connection with leasing space, including broker's leasing commissions or compensation, advertising and other marketing expenses, and legal, space planning, construction, and other expenses incurred in procuring tenants for the Building or renewing or amending leases with existing tenants or occupants of the Building; expenditures for capital improvements, except (1) capital expenditures made primarily for the purpose of reducing operating expense costs or otherwise improving the operating efficiency of the Building and (2) capital expenditures required by law which become effective after the Commencement Date, in either of which cases the cost thereof shall be included in Annual Operating Costs for the calendar year in which the cost shall have been incurred and subsequent calendar years, on a straight line basis, to the extent that such items are amortized over an appropriate period, but not more than ten (10) years, with an interest factor equal to two percent (2%) plus the prime rate (as hereinafter defined) at the time Landlord shall have incurred said costs; costs of other services or work performed for the benefit of other tenants or occupants if the same or similar services are not available to Tenant; any expense for which Landlord actually receives reimbursement from insurance, condemnation awards, other tenants (other than through the payment of additional Annual Operating Costs under such tenants' leases) or any other source; costs incurred in connection with the sale, financing, refinancing, mortgaging, or other change of ownership of the Property or any interest therein; Annual Tax Costs; costs incurred due to a breach by Landlord or

any other tenant of the terms and conditions of any lease; costs of remediating any environmental condition which violates any applicable law; the amount, if any, by which sums paid to entities related to the Landlord for various items and/or services supplied to the Property exceed the cost, if obtained on a competitive basis, of similar items and/or services in the area; management fees in excess of those which are commercially reasonable for comparable properties in the relevant market; costs incurred by Landlord in connection with construction of the Building and related facilities or the correction of latent defects in construction of the Building; expenses resulting from the gross negligence or willful misconduct of Landlord or its agents, employees or contractors; any costs for Landlord's failure to comply with applicable legal requirements; and costs or expenses that are properly chargeable to particular tenants in the Building, including, without limitation, costs and expenses for damages to the Building or any part thereof caused by the act or neglect of another tenant. As used in this Lease, "the prime rate" shall mean the rate of interest per annum announced from time to time by Wells Fargo Bank, N.A. or its successor as its prime lending rate (or if such prime lending rate is discontinued, such comparable rate as Landlord reasonably designates by notice to Tenant).

(ii) If Landlord shall have purchased any item of capital equipment or shall have made any capital expenditure designed to result in savings or reductions in Annual Operating Costs or Tenant Energy Costs applicable to leased space generally, then the costs of having purchased such equipment and such capital expenditures shall be included in Annual Operating Costs for the calendar year in which the costs shall have been incurred and subsequent calendar years, on a straight line basis, to the extent that such items are amortized over such period of time as reasonably can be estimated as the time in which such savings or reductions in Annual Operating Costs are expected to equal Landlord's costs for such capital equipment or capital expenditure, with an interest factor equal to the prime rate at the time of Landlord's having incurred said costs. If Landlord shall have leased any such items of capital equipment designed to result in savings or reductions in Annual Operating Costs, then the rental and other costs paid pursuant to such leasing shall be included in Annual Operating Costs for the calendar year in which they shall have been incurred.

(iii) The term "Base Operating Costs" shall mean the Annual Operating Costs incurred by Landlord during the calendar year 2017. Base Operating Costs shall be calculated based on routine and recurring operations of the Property and shall not include any non-recurring operating costs or repairs related to deferred maintenance which occur less often than once every five (5) years.

(iv) For and with respect to each calendar year of the Term (and any renewals or extensions thereof) excluding, however, the first calendar year during which the Term of this Lease shall have commenced, there shall accrue, as additional rent hereunder, and be paid within thirty (30) days after Tenant's receipt from Landlord of a statement or statements of the amount due, Tenant's proportionate share of the increase, if any, of Annual Operating Costs over Base Operating Costs.

(v) Anything contained in the foregoing provisions of this Article 4 to the contrary notwithstanding, in any instance in which the Tenant shall have agreed in this Lease or otherwise to provide any item or items of Annual Operating Costs partially or entirely at its own expense, in calculating and allocating increases in Annual Operating Costs over Base Operating Costs pursuant to the foregoing provisions of this subsection, Landlord shall make

appropriate adjustments, using reasonable accounting principles, so as to avoid allocating to the Tenant the same such item or items of the Base Operating Costs and Annual Operating Costs (partially or entirely, as aforesaid) being provided to other tenants by Landlord at Landlord's expense. Subject to the preceding sentence, if during all or part of any calendar year, Landlord shall not furnish any item or items of Annual Operating Costs to any portions of the Building because such portions are not occupied or because such item is not required or desired by the tenant of such portion or such tenant is itself obtaining and providing such item or for other reasons, then, for the purposes of computing the additional rent payable hereunder, the amount of Annual Operating Costs for such period (including without limitation in connection with the calculation of Base Operating Costs) shall be deemed to be increased by an amount equal to the additional costs which would normally have been incurred during such period by Landlord if it had at its own expense furnished such item to such portion of the Building.

(f) Annual Tax Costs.

(i) The term "Annual Tax Costs" shall mean all real estate taxes and assessments, general or special, ordinary or extraordinary, foreseen or unforeseen (including "Lease Taxes" as defined in Article 4(j) of this Lease) assessed or imposed upon the Property at the discounted amount (provided that Landlord pays within the discount period, otherwise such amount shall be calculated based upon the undiscounted amount), plus the expenses of any contests (administrative or otherwise) of tax assessments or proceedings to reduce taxes, including reasonable attorneys' and appraisers' fees, incurred each calendar year during the Term (and any renewals or extensions thereof) including, without limit, the first calendar year during which the Term of this Lease shall have commenced; provided however, that except as set forth in the next sentence, there shall be excluded from Taxes all income taxes, excess profit taxes, excise taxes, franchise taxes, estate, succession, inheritance and transfer taxes. If, due to a future change in the method of taxation, any franchise, income, profit or other tax, however designated, shall be levied or imposed in substitution, in whole or in part, for (or in lieu of) any tax or addition or increase in any tax which would otherwise be included within the definition of Taxes, such other tax shall be deemed to be included within Taxes as defined in this Lease. For all purposes under this Lease, "Annual Tax Costs" shall not include (1) penalties, fines or interest incurred as a result of Landlord's inability or failure to make payment of Annual Tax Costs (unless directly caused by Tenant) and/or to file any tax or informational returns when due, or from Landlord's failure to make any payment of Annual Tax Costs required to be made by Landlord hereunder before delinquency, (2) taxes to be paid directly by Tenant, whether or not actually paid, and (3) transfer or other taxes incurred in the sale, financing or refinancing of the Premises or the Building. Tax refunds shall be credited against Annual Tax Costs and promptly refunded to Tenant regardless of when received, based on the year to which the refund is applicable.

(ii) The term "Base Tax Costs" shall mean the Annual Tax Costs incurred by Landlord during the calendar year 2017 (excluding the expenses of any contests (administrative or otherwise) of tax assessments or proceedings to reduce Annual Tax Costs, including attorneys' and appraisers' fees incurred in the calendar year 2017). If Base Tax Costs are subsequently reduced by an assessment appeal or otherwise, then Landlord shall retroactively reduce Base Tax Costs for purposes of determining additional rent; provided, however, that any such reduction shall be made and written notice thereof given to Tenant no later than the date

that is five (5) years after the last calendar day of the calendar year for which the reduction is made.

(iii) For and with respect to each calendar year of the Term (and any renewals or extensions thereof) excluding, however, the first calendar year during which the Term of this Lease shall have commenced, there shall accrue, as additional rent hereunder, and be paid within fifteen (15) days after Landlord shall have given to Tenant a statement or statements of the amount due, Tenant's proportionate share of the increase, if any, of Annual Tax Costs over Base Tax Costs.

(g) Partial Year. If only part of any calendar year shall fall within the Term, the amount computed as additional rent with respect to such calendar year shall be prorated in proportion to the portion of such calendar year falling within the Term (but the expiration or termination of the Term prior to the end of such calendar year shall not impair the Tenant's obligation under this Lease to pay such prorated portion of such additional rent with respect to that portion of such year falling within the Term, which shall be paid within thirty (30) days after Tenant's receipt of a statement or statements of the amount due.

(h) Payment of Estimated Increase. Anything in this Lease to the contrary notwithstanding, the Landlord shall be entitled to make from time to time during the Term, a reasonable estimate of the amount of Tenant's proportionate share of the increase, if any, of Annual Operating Costs over Base Operating Costs and Tenant's proportionate share of the increase, if any, of Taxes over Base Tax Costs which may become due under this Lease with respect to any calendar year and to require the Tenant to pay to the Landlord, at the time and in the manner in which the Tenant is required under this Lease to pay the monthly installment of the Fixed Rent with respect to such month, with respect to each calendar month during any such calendar year, one-twelfth (1/12) of the amount which Landlord shall have estimated will become payable on account of increases in Annual Operating Costs and Annual Tax Costs. In such event, Landlord shall cause the actual amount of the additional rent to be computed and a statement thereof and of Base Operating Costs and Base Tax Costs to be sent to the Tenant within one hundred twenty (120) days following the end of the calendar year (including the last calendar year of the Term); the Tenant or the Landlord, as the case may be, shall, within thirty (30) days after such statement is received by Tenant, pay to the other the amount of any deficiency or overpayment, respectively, therein.

(i) Disputes. Any statement furnished to Tenant by Landlord under the preceding paragraph or other provisions of this Article shall constitute a final determination as between Landlord and Tenant of the additional rent due from Tenant for the period represented thereby unless Tenant, within sixty (60) days after a statement is furnished, shall have given a notice to Landlord that Tenant disputes the correctness of the statement, specifying in reasonable detail the basis for such assertion (the "Audit"). Pending resolution of such a dispute, Tenant shall pay the additional rent in accordance with the statement furnished by Landlord. Landlord agrees, upon prior written request, during normal business hours to make available for inspection by an independent certified public accountant, not compensated on a contingency basis, at Landlord's offices, Landlord's books and records which are relevant to any items in dispute. If, after the Audit, Tenant disagrees with Landlord's calculation of such costs, Tenant shall, within thirty (30) days of completion of the Audit (but not later than one hundred fifty (150) days of Tenant's receipt of Landlord's Statement) so advise Landlord in writing and shall specify the

reason for such disagreement. If Landlord and Tenant are unable to resolve such disagreement in good faith within thirty (30) days of Landlord's receipt of such notice, Landlord and Tenant shall select a mutually agreeable certified public accountant (the "Expert"), who will review all information supplied to and by Tenant in connection with said disputed item(s) and determine the amount of the overpayment, if any. The findings of such Expert shall be binding on both parties and not subject to appeal. If the Expert determines that Tenant's ultimate liability for Annual Operating Cost and, Annual Tax Costs does not equal the aggregate amount actually paid by Tenant to Landlord during the period which is the subject of the Audit, the appropriate adjustment shall be made between Landlord and Tenant, and any payment required to be made by Landlord or Tenant to the other shall be made within thirty (30) days after the Expert's final, written determination. If the Expert determines that there is an overcharge for any twelve month period of more than 5% of the amount invoiced by Landlord for such period, Landlord shall pay the costs of the Expert. Before conducting the Audit, Tenant must pay the full amount of Tenant's Proportionate Share of Annual Operating Costs and Annual Tax Costs then in question. In no event shall this Lease be terminable nor shall Landlord be liable for damages based upon any disagreement regarding an adjustment of Annual Operating Costs, except as otherwise expressly set forth in this subsection (i). Tenant agrees that the results of any audit shall be kept strictly confidential by Tenant and shall not be disclosed to any nonaffiliated person or entity.

(j) Lease Tax. If federal, state or local law now or hereafter imposes any tax, assessment, levy or other charge (other than any income tax) directly or indirectly upon the Landlord with respect to this Lease or the value thereof, or upon the Tenant's use or occupancy of the Premises, or upon the rent, additional rent or any other sums payable under this Lease or upon this transaction, except if and to the extent that the same are included in the Annual Tax Costs (all of which are herein called "Lease Taxes") the Tenant shall pay to the Landlord, as additional rent hereunder and upon demand, the amount of such tax, assessment, levy or other charge, unless the Tenant shall be prohibited by law from paying such tax, assessment levy or other charge, in which event the Landlord shall be entitled, at its election, to terminate this Lease, to be effective no sooner than twelve (12) months thereafter, by written notice to the Tenant delivered no later than six (6) months after the effectiveness of such change in the tax laws.

5. **Covenant to Pay Rent and Additional Rent; Late Charge**.

Tenant shall, without prior demand, notice, setoff or deduction (except as otherwise expressly set forth in this Lease), pay the Fixed Rent and all other sums which may become due and payable by Tenant under this Lease, at the times, at the places and in the manner provided in this Lease. All such other sums shall be payable as additional rent for all purposes whether or not they would otherwise be considered rent. If any payment or any part thereof to be made by Tenant to Landlord pursuant to the terms of this Lease shall have become overdue for a period in excess of ten (10) days, a late charge of five cents ($.05) for each dollar so overdue may be charged by Landlord for the purpose of defraying the expense incident to handling such delinquent payment, together with interest from the date when such payment or part thereof was due at the Lease Interest Rate (defined below) or such lesser amount or rate, if any, as represents the maximum amount or rate Landlord lawfully may charge in respect of Tenant in such circumstances. Nothing herein shall be construed as waiving any rights of Landlord arising out of any uncured defaults of Tenant (following applicable notice and cure periods) by reason of Landlord's assessing or accepting any such late payment, the late charge and interest provided herein is separate and apart from any rights relating to remedies of the Landlord after uncured

default (following applicable notice and cure periods) by Tenant in the performance or observance of the terms of this Lease. Without limiting the generality of the foregoing, if an uncured Event of Default exists, Landlord may (but shall not be obligated to do so), in addition to any other rights it may have in law or equity, cure such default on behalf of Tenant and Tenant shall reimburse Landlord upon demand for any sums paid or costs reasonably incurred by Landlord in curing such default, including interest thereon at the Lease Interest Rate or such lesser rate as represents the maximum rate Landlord lawfully may charge in respect of Tenant in such circumstances, reasonable attorney's fees and other legal expenses, including also the said late charge and interest on all sums paid and costs reasonably incurred by Landlord as aforesaid, which sums and costs together with late charge and interest thereon shall be deemed additional rent hereunder. As used in this Lease, the "Lease Interest Rate" shall mean four percent (4%) plus the prime rate.

6. **Use**.

The Premises are to be used only by Tenant for general office purposes, as well as a light laboratory/research on the first floor Premises, if applicable, and for other legally permitted uses incidental thereto. Tenant shall not use or occupy the Premises or any part thereof, or permit the Premises or any part thereof to be used or occupied, other than as specified in the sentence immediately preceding. Tenant shall permit its employees, invitees and guests to park only automobiles, or similarly sized vehicles, on the Property. Such parking shall be provided at a rate of 3.7 spaces/1,000 rsf and shall be unreserved and be limited to Tenant's proportionate share of the Building.

7. **Assignment and Subletting**.

(a) The Tenant shall not mortgage, pledge or encumber this Lease. Except in connection with a Permitted Transfer (as hereinafter defined), the Tenant shall not assign this Lease or sublet or underlet the Premises or any part thereof, or permit any other person or entity to occupy the Premises or any part thereof, without on each occasion first obtaining the written consent thereto of the Landlord. An assignment within the meaning of this Lease is intended to comprehend not only the voluntary action of Tenant, but also any levy or sale on execution or other legal process against Tenant's goods or other property of the leasehold, and every assignment of assets for the benefit of creditors, and the filing of any petition or order or any adjudication in bankruptcy or under any insolvency, reorganization or other voluntary or compulsory procedure, and the calling of a meeting of creditors, and the filing by or against Tenant of any petition or notice for a composition with creditors, and any assignment by operation of law. For purposes of the foregoing, a transfer, by any person or persons controlling the Tenant on the date hereof, of such control to a person or persons not controlling the Tenant on the date hereof shall be deemed to be an assignment of this Lease; provided however, the foregoing shall not apply to any transfers of interests that are traded on a national exchange.

(b) Except in connection with a Permitted Transfer, if Tenant proposes to assign this Lease or sublet all or any portion of the Premises, Tenant shall, prior to the proposed effective date thereof (the "Effective Date"), deliver to Landlord a copy of the proposed agreement and all ancillary agreements with the proposed assignee or subtenant, as applicable. Landlord shall then have all the following rights, any of which Landlord may exercise by written

notice to Tenant given within thirty (30) days after Landlord receives the foregoing documents (a "Landlord Notice"):

(i) With respect to a proposed assignment of this Lease, the right to terminate this Lease on the Effective Date as if it were the Expiration Date, upon which termination all of Tenant's obligations under this Lease shall expire; provided, however, Tenant shall have the right, by written notice to Landlord given within five (5) days after the date of Tenant's receipt of the Landlord Notice, to rescind its request for consent to an assignment, in which event the Lease shall continue in full force and effect;

(ii) With respect to a proposed subletting of the entire Premises, the right to terminate this Lease on the Effective Date as if it were the Expiration Date, upon which termination all of Tenant's obligations under this Lease shall expire; provided, however, Tenant shall have the right, by written notice to Landlord given within five (5) days after the date of Tenant's receipt of the Landlord Notice, to rescind its request for consent to a sublease, in which event the Lease shall continue in full force and effect;

(iii) With respect to a proposed subletting of 50% or more of the area of the Premises, the right to terminate this Lease as to the portion of the Premises affected by such subletting on the Effective Date, as if it were the Expiration Date, in which case Tenant shall promptly execute and deliver to Landlord an appropriate modification of this Lease in form satisfactory to Landlord in all respects; provided, however, Tenant shall have the right, by written notice to Landlord given within five (5) days after the date of Tenant's receipt of the Landlord Notice, to rescind its request for consent to a proposed sublease, in which event the Lease shall continue in full force and effect; or

(iv) Landlord may consent to the proposed assignment or sublease on such terms and conditions as Landlord may reasonably require, including without limitation, the execution and delivery to Landlord by the assignee of an assumption of liability agreement in form reasonably satisfactory to Landlord, including an assumption by the assignee of all of the obligations of Tenant and the assignee's ratification of an agreement to be bound by all of the provisions of this Lease, including the warrants of attorney to confess judgment in assumpsit and in ejectment; or, in the case of a sublease, the execution and delivery by the subtenant of a written agreement with Landlord, in such form and with such terms, covenants and conditions as may be reasonably required by Landlord; or

(v) Landlord may withhold its consent to the proposed assignment or sublease, provided, however, that if Landlord declines to exercise one of the options set forth in items (i) through (iii) above, that Landlord will not unreasonably withhold its consent so long as the identity, reputation and financial strength of the proposed assignee or subtenant, and the proposed use of the Premises, are reasonably acceptable to Landlord; provided further, however, that Landlord shall in no event be required to consent to any sublease of space for rent and other charges less than those that the sublessor is required to pay or any assignment or subletting to a proposed assignee or subtenant that is (w) a government or any subdivision, agency or instrumentality thereof, (x) a school, college, university or educational institution of any type (whether for profit or non-profit), (y) an employment, recruitment or temporary help, service or agency or (z) another tenant of Landlord in Chesterbrook Corporate Center® or Glenhardie

Corporate Center® if Landlord has suitable space available for rent in Chesterbrook Corporate Center® or Glenhardie Corporate Center®.

(vi) In the event that Landlord does consent to the assignment or subletting, Tenant shall have ninety (90) days from its receipt of Landlord's notice thereof to enter into the proposed sublease or assignment with the prospective subtenant or assignee described in Tenant's notice to Landlord. If such sublease or assignment has not been executed within such time period and with such identified assignee or subtenant, the consent given by Landlord shall be considered to have been withdrawn.

(c) No assignment or sublease, whether with or without the Landlord's consent, shall in any way relieve or release the Tenant from liability for the performance of all terms, covenants and conditions of this Lease.

(d) Except in the event of a Permitted Transfer, in the event of any sublease or assignment by Tenant of its interest in the Premises or this Lease or any portion thereof, whether or not consented to by Landlord, each monthly installment of Fixed Rent payable hereunder with respect to the Premises or the portion thereof subject to such subletting or assignment shall be increased by an amount equal to (i) in the case of any subletting, the Excess Rent (defined below) for such portion; and, in the case of any assignment, the Excess Rent payable by the assignee as amortized on a monthly basis over the remaining Term of this Lease with interest at the Lease Interest Rate (defined at Article 5 hereof). As used herein, "Excess Rent" shall mean a sum equal to fifty percent (50%) of the amount by which the rent and other charges or other consideration paid to Tenant by any subtenant or assignee exceeds the pro rata portion, for each month of such subletting or assignment, of the Fixed Rent and additional rent for such space then payable for such month by Tenant to Landlord pursuant to the provisions of this Lease in the absence of this subsection (d), less the portion applicable to such month, when amortized from the dates incurred over the remaining term of the sublease or assignment, of Tenant's cost of improvements made or paid for by Tenant to satisfy the needs of the subtenant, and legal fees, leasing commissions and similar capital costs incurred by Tenant in connection with the assignment or subletting.

(e) If, pursuant to the exercise of the Landlord's option in 7(b)(iii) above, this Lease terminates as to only a portion of the Premises, the Fixed Rent and Tenant's Proportionate Share for the additional rent shall be adjusted in proportion to the portion of the Premises affected by such termination, as determined by Landlord; and Tenant, within thirty (30) days after Tenant's receipt of written demand therefor and any supporting documentation reasonably requested by Tenant, shall pay to Landlord Landlord's actual documented cost of any alterations necessary to separate such portion of the Premises from the remainder of the Premises plus three percent (3%) for Landlord's overhead.

(f) If Landlord exercises any of its options under section 7(b)(i), (ii) or (iii), Landlord may then lease the Premises or any portion thereof to Tenant's proposed assignee or subtenant, as the case may be, without liability whatsoever to Tenant.

(g) In the event Landlord fails to respond to any request for consent to an assignment, sublease or other transfer within ten (10) business days, Tenant shall have the right to provide Landlord with a second request for consent to such assignment, sublease or other

transfer. If Landlord's failure to respond continues for five (5) business days after its receipt of such second request for consent, the assignment, sublease or other transfer for which Landlord has submitted a request for consent shall be deemed to have been consented to by Landlord. Tenant's second request for consent must specifically state that Landlord's failure to respond within a period of five (5) business days shall result in the subject assignment, sublease or other transfer being deemed to have been consented to by Landlord.

(h) In addition to, and not in lieu of, any other rights and remedies available to Landlord therefor, Landlord shall have the right to terminate this Lease if Tenant assigns or underlet the Premises without first obtaining Landlord's written consent in violation of this Lease. In the event that Landlord exercises said right to terminate, said termination shall become effective on the date set forth in Landlord's written notice.

(i) Tenant shall pay Landlord, as additional rent, a reimbursement for all reasonable and actual expenses incurred by Landlord, including counsel fees, in connection with Landlord's review of any subletting or assignment request from Tenant, irrespective of Landlord's election to approve or deny such request, not to exceed $2,500 per occurrence.

(j) Notwithstanding the foregoing, Tenant may assign its entire interest under this Lease or sublet the Premises (i) to any entity controlling or controlled by or under common control with Tenant or (ii) to any successor to Tenant by purchase, merger, consolidation or reorganization (hereinafter, collectively, referred to as "Permitted Transfer") without the consent of Landlord, provided: (1) no Event of Default exists; (2) if such proposed transferee is a successor to Tenant by purchase, said proposed transferee shall acquire all or substantially all of the stock or assets of Tenant's business or, if such proposed transferee is a successor to Tenant by merger, consolidation or reorganization, the continuing or surviving entity shall own all or substantially all of the assets of Tenant; and (3) with respect to a Permitted Transfer to a proposed transferee described in clause (ii), such proposed transferee shall have a net worth which is at least equal to Tenant's net worth immediately preceding the execution of this Lease.

8. **Condition of Premises; Improvement of the Premises**.

(a) Except as otherwise expressly set forth herein, the Premises is leased to Tenant in its current AS-IS, WHERE-IS CONDITION; provided that Landlord shall, at Landlord's sole cost and expense using Building standard finishes, complete the renovation of the bathrooms and common areas (hallway carpeting) on the second floor of the Building (matching, as near as practicable, standards existing on the first floor of the Building and in compliance with all applicable building codes and regulations) prior to the Commencement Date (collectively, the "Base Building Work").

(b) Tenant Improvements.

(i) Construction of Tenant Improvements. Tenant will have plans for improvements to the Premises designed and approved in accordance with Section 8(b)(ii) (the "Tenant Improvements") and constructed by Landlord as construction manager in accordance with Sections 8(b)(iii) and (iv).

(ii) Tenant Improvement Plans. Tenant's specifications and plans for the Tenant Improvements shall be prepared by Tenant's architect and provided to Landlord not

later than January 30, 2017, and Landlord's approval or denial of such plans to be communicated to Tenant within ten (10) business days of such delivery. The tenant improvement plans will be prepared in commercially reasonable sufficient detail to permit Tenant or Landlord to construct the Tenant Improvements, and shall include partition layout (dimensioned), door location and door schedule including hardware, reflected ceiling plan, telephone and electrical outlets with locations (dimensioned), special electrical, HVAC and/or plumbing work, mechanicals, special loading requirements, such as the location of file cabinets and special equipment, openings in the walls or floors, all necessary sections and details for special equipment and fixtures, furniture layout and finishes including, without limitation, carpentry and millwork, floor coverings, wall coverings, color schedules, and any other special finishes. The tenant improvement plans shall be prepared in accordance with applicable laws and code requirements. Landlord shall not unreasonably withhold, condition or delay its approval of the tenant improvement plans. Any comments or suggested changes of Landlord shall be in writing and may be noted on the applicable drawings and plans provided they are legible and sufficiently detailed as warranted under the circumstances, including specific references and notations on applicable drawings and plans to highlight areas in which changes are requested. Tenant shall respond to any comments or suggested changes within five (5) business days of receipt from Landlord. Any comments or suggested changes of Tenant shall be in writing and may be noted on the applicable drawings and plans provided they are legible and sufficiently detailed as warranted under the circumstances, including specific references and notations on applicable drawings and plans to highlight areas in which changes are requested. Landlord shall then have five (5) business days to approve or deny such plans. This procedure shall be repeated with the parties working in good faith to resolve any differences until the Tenant construction plans are finally approved by Landlord and written approval has been delivered to and received by Tenant. A "Tenant Review Day" is any full business day during which the tenant improvement plans awaits review, approval, and/or comments from Tenant following Landlord's submission to Tenant for review. After the eleventh (11th) total Tenant Review Day, each such subsequent Tenant Review Day shall constitute a Tenant Delay. Upon approval by Landlord, the tenant improvement plans shall become final and shall not be changed except as set forth herein and without Landlord's and Tenant's further approval, which shall not be unreasonably withheld, conditioned or delayed (as finally approved, the "Tenant Improvement Plans"). Upon approval of the Tenant Improvement Plans, Landlord shall specify those Tenant Improvements (including laboratory improvements) which Tenant must remove from the Premises upon termination of the Lease.

(iii) Changes to Plans. Tenant shall be permitted from time to time to direct changes in the Tenant Improvement Plans after the approval of the Tenant Improvement Plans in accordance with the procedures set forth herein.

(A) Any request for any changes to the Tenant Improvement Plans by Tenant must be presented by Tenant to Landlord and its general contractor in writing (each, a "Change Order Request"). Within five (5) business days of its receipt of any Change Order Request, (1) Landlord and/or its general contractor shall prepare a written proposal of the cost and time impacts to implement the Change Order Request ("Price/Time Adjustment"), or (2) if Landlord and/or the General Contractor reasonably believes that the Change Order Request does not comply with the applicable laws, Lease, applicable regulations or the insurance requirements, or Landlord does not approve the Change Order Request on some other basis, Landlord and/or its general contractor shall request revisions or modifications thereto.

(B) If the Landlord and its general contractor have reviewed the Change Order Request and responded with the Price/Time Adjustment proposal for the Change Order Request, the Tenant shall expeditiously (within two (2) business days) respond as to its acceptance or rejection of the Price/Time Adjustment. Tenant's failure to timely respond shall be deemed a rejection of the Price/Time Adjustment.

(C) If the Landlord requests revisions or modifications pursuant to this Article and the Tenant wishes to proceed with the Change Order Request, then Tenant shall submit such revisions or modifications within two (2) business days after its receipt of such request from Landlord or its general contractor. Within five (5) business days following receipt by Landlord and its general contractor of such revisions or modifications, Landlord and its general contractor shall review such modifications and shall give its written response thereto, including any Price/Time Adjustment, or shall request other revisions or modifications thereon. The preceding two sentences shall be implemented repeatedly until Landlord and its general contractor and Tenant give written approval to the Change Order Request or Tenant withdraws the Change Order Request. An approved Change Order Request shall be referred to as a Change Order once approved by the Tenant, Landlord and its general contractor.

(D) For any Change Order for which Tenant accepted the Price/Time Adjustment set forth herein, the final Price/Time Adjustment shall be equal to the amount and time so set forth and will be binding on Landlord, General Contractor and Tenant, and any Price/Time Adjustment resulting from a Change Order shall increase the general contract lump sum and/or Project schedule.

(iv) Completion by Landlord as Construction Manager. Landlord as construction manager will solicit competitive bids for the construction of the Tenant Improvements from the following contractors and Landlord will enter into a construction contract with one of such contractors as determined by Landlord in its sole discretion, but after consultation from Tenant: McLucas; Shields; LK Miller; and HSC Builders. The construction contract entered into with the selected general contractor shall be at a fixed, lump sum amount, and shall also include a detailed schedule for construction of the Tenant Improvements acceptable to Landlord and Tenant. Landlord shall be paid an administrative and construction management fee for Landlord's supervision of such construction in an amount equal to $41, 750.00 (the "Project Management Fee"), which management fee shall remain fixed and not subject to change for the project except for increases equal to two percent (2%) of the net cost increase or decrease resulting from any Change Order. Landlord shall ensure that the general contractor (1) is qualified and licensed (as necessary); (2) is fully competent to timely and properly perform the services or work to be performed; (3) will be engaged under industry standard terms and conditions (including warranties, payment procedures, indemnity, Change Orders, waiver of liens, schedule of values, etc., but excluding bonding) and at industry compatible rates; (4) will comply in all respect to the requirements of this Lease and the Tenant Improvement Plans; and (5) will carry and maintain appropriate commercial general liability and other insurance satisfactory to Landlord.

(v) Delay in Substantial Completion of the Tenant Improvements. Landlord shall use good faith diligent efforts to cause the Tenant Improvements to be Substantially Completed not later than July 1, 2017, subject to force majeure and Tenant Delays. If the Premises are not delivered to Tenant with the Tenant Improvements Substantially

Completed by August 29, 2017, Tenant will receive a credit against Fixed Rent for each day from August 15, 2017, as such date is extended for each day of force majeure and Tenant Delay occurring from the date of this Lease, until the date of Substantial Completion (as extended, the "Rent Credit Date").

(vi) Tenant Delay. For purposes of determining the date when the Premises are ready for occupancy (and, correspondingly, the date of Substantial Completion of the Tenant Improvements, the Commencement Date and the Rent Credit Date), there shall not be considered the duration of any delay ("Tenant Delay") which is caused by:

(A) changes in the work to be performed by Landlord in readying the Premises for Tenant's occupancy, which changes shall have been requested by Tenant after the approval by Landlord and Tenant of the Tenant Improvement Plans;

(B) delays, not caused by Landlord, in furnishing materials or procuring labor required by Tenant for installations or work in the Premises including but not limited to laboratory components of the Tenant Improvements;

(C) any failure by Tenant to furnish any required plan, information, approval or consent within the required period of time (including, without limit, delivery of the Tenant Improvement Plans not later than January 30, 2017); or

(D) the performance of any work or activity in the Premises by Tenant or any of its employees, agents or contractors.

The Tenant Improvements shall be deemed Substantially Complete and the Commencement Date shall occur on the date the Premises would have been ready for occupancy but for the causes described in this subparagraph.

(vii) Construction Standards, Punchlist, Substantial Completion. All construction shall be done in a good and workmanlike manner, shall be free from defects and deficiencies, shall comply at the time of completion with all applicable laws and requirements of the governmental authorities having jurisdiction, and shall be in accordance with the Tenant Improvement Plans. Tenant shall have the right to inspect the Tenant Improvements at all reasonable times during business hours upon written notice and request to Landlord, provided however, Tenant shall not destroy or damage any such work in place, and that Tenant's failure to inspect the Tenant Improvements shall in no event constitute a waiver of any of Tenant's rights hereunder nor shall Tenant's inspection of the Tenant Improvements constitute Tenant's approval of the same. Tenant may attend construction project meetings and, in connection with its monitoring of the construction, will be provided with copies of meeting minutes, payment applications and payments, schedules, inspection reports, punchlists, and other construction records upon their distribution. Landlord shall provide a certificate of occupancy to Tenant upon Substantial Completion of the work. However, prior to the Premises being delivered to Tenant and the commencement of the Term, a representative of Landlord and a representative of Tenant shall walk through the Premises and jointly prepare a list of items which, in the mutual opinion of Landlord and Tenant, have not been fully completed or which require repair by the general contractor (the "Punchlist Items"), which list may be supplemented jointly by Landlord and Tenant. Landlord shall use reasonable commercial efforts to cause the general contractor to

complete or repair the Punchlist Items within thirty (30) days after the date of the "walk-through," or, if such Punchlist Items cannot reasonably be completed or repaired within thirty (30) days, shall use commercially reasonable efforts to complete or repair such items as quickly as possible and at minimal interruption to Tenant. For purposes of this Lease, "Substantial Completion" of the Tenant Improvements shall be the date all of the following conditions are satisfied, or an earlier date by which such conditions would have been satisfied but for delays caused solely by Tenant, including but not limited to any delay in providing Tenant's specifications and plans for the Tenant Improvements and Tenant's Change Orders: (1) Landlord notifies Tenant in writing that the general contractor has substantially completed the Tenant Improvements, leaving only Punchlist Items remaining; (2) Landlord provides to Tenant a certificate from Landlord's engineer or general contractor attesting to such Substantial Completion in the customary form, and signed by Landlord; (3) a conditional or permanent certificate of occupancy has been issued by the applicable regulatory authority for the Premises as they relate to the Tenant Improvements that permits Tenant's occupancy and use of the Premises for the purposes contemplated by the Lease; (4) the other portions of the building and the Premises, including the loading dock, are accessible to Tenant via the lobby, entranceways, elevators and hallways as permitted under the Lease; (5) the Premises are broom clean; and (6) the building systems (i.e., base building mechanical, electrical, life safety, plumbing, sprinkler systems and HVAC systems) are in good working order and repair.

(viii) Warranty. Landlord shall ensure that the general contract contains a warranty by the general contractor that when completed, the Tenant Improvements will be free and clear of material defects in workmanship and material for one year after Substantial Completion of the Tenant Improvements, and that general contractor will correct free of charge during this warranty period any material defect within thirty (30) days of its receipt of a notice from Landlord of such defect (with customary exceptions and exclusions for normal wear and tear, etc.); provided, however, that if a defect is of such a nature that the same cannot be corrected completely within said thirty (30) day period, then general contractor will commence correcting the defect within said thirty (30) day period and proceed diligently and in good faith to completely correct the defect. Landlord will use commercially reasonable efforts to cooperate with Tenant and to enforce such warranties upon notice of any claim by Tenant, or alternatively Landlord may assign such warranties to Tenant.

(ix) Tenant Improvement Costs. Tenant shall, subject to Section 8(b)(x) below, be responsible for and pay the costs, expenses and fees incurred for the construction of the Tenant Improvements, including without limitation (1) Tenant's architectural, engineering and design costs associated with the Tenant Improvements, (2) the cost charged to Landlord or Tenant by the general contractor and all subcontractors for performing construction of the Tenant Improvement, (3) the cost to Landlord of directly performing any part of the construction of the Tenant Improvements, (4) the Project Management Fee, (5) construction permit fees, (6) costs of built-in furniture that is part of the Tenant Improvement Plans, (7) mechanical and structural engineering fees for the Tenant Improvements, and (8) Tenant's cabling and costs of moving furniture and equipment into and within the Building (together, the "Tenant Improvement Costs"). Notwithstanding Tenant's responsibility to Landlord for the Tenant Improvement Costs associated with the Landlord's general contractor for work to construct the Tenant Improvements, Landlord shall be responsible for direct payments to its general contractor under the general contract with no recourse to Tenant.

(x) Tenant Allowance. Landlord shall provide an allowance to Tenant equal to $1,703,730.00 (the "Tenant Allowance"), which Tenant Allowance shall be applied by Landlord to the payment of the Tenant Improvements Costs; any remaining balance may be used by Tenant for any costs or expenses related to or arising from the design, construction, permitting, general conditions, management and inspection of the Tenant Improvements and tenant improvements for any Expansion Space (as defined in Section 40) but only if expended within 365 days from the Commencement Date defined in Section 3(a). In addition, and not as part of the Tenant Allowance, Landlord shall pay for the preparation of one test fit plan to be prepared by Tenant's architect up to an amount of $3,903.68 (the "Test Fit Allowance"). Upon submission of an invoice evidencing completion of the test fit plan by Tenant's architect, Landlord shall pay such architect an amount equal to the lesser of the invoiced amount or the Test Fit Allowance. Any excess payment required by the architect shall be paid by Tenant.

(xi) Payment for Tenant Improvement Costs. If there is a projected excess of Tenant Improvement Costs based upon the budget for the Tenant Improvements, Tenant agrees to prepay such projected excess to Landlord within ten (10) days of being billed therefor, even though such costs have not been incurred. Upon completion of the Tenant Improvements by Landlord, Tenant shall pay to Landlord all costs incurred in excess of the Tenant Allowance, which were not previously paid by Tenant to Landlord, or Landlord shall reimburse to Tenant any amount of the projected costs of the Tenant Improvements prepaid by Tenant to Landlord which were not actually expended by Landlord for the Tenant Improvements. The Tenant Allowance shall be released by Landlord as follows:

(c) Direct Tenant Work. Notwithstanding anything herein, Tenant's furniture, security, telephone and data wiring and cabling (hereinafter called the "Direct Tenant Work") shall be installed in accordance with the Tenant Improvement Plans by contractors contracting with Tenant and not with Landlord.

(d) Access; Acceptance of Work. Landlord shall afford Tenant and its employees, agents and contractors access to the Premises, at reasonable times prior to the Commencement Date and at Tenant's sole risk and expense, in accordance with **Exhibit "D"** ("Early Access by Tenant").

(e) Representations and Warranties. Landlord represents and warrants to Tenant that (i) the Building is not subject any covenants, encumbrances, conditions, restrictions, private agreements, reciprocal easement agreements or any other exceptions to title which prohibits or limits Tenant's ability to use the Building and Premises for the purposes described in this Lease (collectively, the "Encumbrances"), (ii) the Property is not in violation of the Encumbrances; (iii) the Property (including the Building and Premises) is presently (and will be as of the Commencement Date) in compliance with all laws (including, but not limited to, the Americans with Disabilities Act), Encumbrances and fire underwriter's requirements; (iv) there are no outstanding delinquent real estate taxes or assessment for the Building; (v) the Building is not subject to any pending, or, to Landlord's knowledge threatened litigation; (vi) Landlord holds fee simple title to the Building; and (vii) the Premises are not leased and are not subject to any rights of first refusal, rights of first offer, options or other preferential rights to lease, occupy, license or purchase. Landlord makes no representations or warranties with respect to the zoning of the Premises or Tenant's intended use of the Premises.

9. **Alterations**.

No alterations, additions or improvements (excluding cosmetic work, as set forth herein) shall be made to the Premises or any part thereof by or on behalf of Tenant without first submitting a detailed description thereof to Landlord and obtaining Landlord's written approval. In the event Landlord fails to respond to any request for consent to an alteration within ten (10) business days, Landlord shall be deemed to have denied such requested alteration. Cosmetic work (such as painting and carpeting) is permitted without Landlord's consent provided the same shall not exceed $50,000.00 in the aggregate in any twelve (12) month period. For any alterations, additions or improvements affecting structural portions of the Building or any Building systems, Landlord, at Landlord's option, shall have the right to provide construction management for and on behalf of Tenant at Tenant's sole expense constituting five percent (5%) of the alteration's total cost. All alterations, additions or improvements made by Tenant and all fixtures attached to the Premises shall become the property of Landlord and remain at the Premises or, at Landlord's option, after written notice to Tenant, any or all of the foregoing which may be designated by Landlord shall be removed at the cost of Tenant before the expiration or sooner termination of this Lease and in such event Tenant shall repair all damage to the Premises caused by the installation or removal; provided that Tenant may submit a written request to Landlord at the time of seeking Landlord's approval for any alteration, addition or improvement requesting a determination by Landlord as to whether such alteration, addition or improvement will need to be removed at the expiration or sooner termination of the Lease in which event Landlord's determination shall be shall be binding. Notwithstanding anything in this Lease, unless otherwise requested by Landlord in writing, Tenant shall remove all Direct Tenant Work (defined at Article 8(b) hereof) and shall repair all damage to the Premises caused by the installation or removal of such Direct Tenant Work. Except as set forth in Article 16(b)(viii), Tenant shall not erect or place, or cause or allow to be erected or placed, any sign, advertising matter, lettering, stand, booth, showcase or other article or matter in or upon the Premises and/or the building of which the Premises are a part, without the prior written consent of Landlord, not to be unreasonably withheld; provided however, Tenant may place such items within the Premises so long as not visible from the exterior of the Premises. Tenant shall not place weights anywhere beyond the safe carrying capacity of the structure.

10. **Rules and Regulations**.

The rules and regulations attached to this Lease as **Exhibit "E"**, and such additions or modifications thereof as may from time to time be made by Landlord upon written notice to Tenant, shall be deemed a part of this Lease, as conditions, with the same effect as though written herein, and Tenant also covenants that said rules and regulations will be faithfully observed by Tenant, Tenant's employees, and all those visiting the Premises or claiming under Tenant. All such changes to rules and regulations will be reasonable and will be generally applicable to all tenants of the Building and shall be sent by Landlord to Tenant in writing. In the event of a conflict between the rules and regulations and the terms of this Lease, the terms of this Lease shall control. Landlord shall not knowingly enforce the rules and regulations against Tenant in a discriminatory manner.

11. **Fire or Other Casualty**.

(a) If, during the term of this Lease, or any renewal or extension thereof, the Building is so damaged by fire or other casualty that the Premises are rendered unfit for occupancy (whether or not the Premises are damaged), Landlord shall deliver notice to Tenant of the estimated time to repair the damage within sixty (60) days after the date of such fire or other casualty (the "Repair Estimate"). If the Repair Estimate provides that the damage cannot be repaired within two hundred seventy (270) days from the casualty, then either Landlord or Tenant may terminate this Lease upon written notice to the other given within thirty (30) days after the Repair Estimate is delivered by Landlord to Tenant, which termination shall be effective as of the date of the occurrence of such damage, and Tenant shall pay the rent apportioned to the time of such termination and Landlord may enter upon and repossess the Premises without further notice. If neither Landlord or Tenant elects to terminate the Term of this Lease, Landlord, subject to reasonable delays for insurance adjustments and to delays caused by matters beyond Landlord's reasonable control, will repair whatever portion, if any, of the Premises or of the Building serving the Premises which may have been damaged and Landlord may enter and possess the Premises for that purpose; while the Tenant is deprived of the Premises, the Fixed Rent shall be suspended in proportion to the number of square feet of the Premises rendered untenantable. Such restoration shall be to substantially the same condition prior to the casualty, except for modifications required by applicable laws or by Landlord's lender. If the Premises or the Building shall be damaged so that such damage does not render any portion of the Premises unfit for occupancy, Landlord will repair whatever portion, if any, of the Premises or of the Building serving the Premises which may have been damaged and Tenant will continue in possession and rent will not be apportioned or suspended. Notwithstanding any other provisions of this Article 11, (a) Landlord shall have no duty to repair or replace any personal property, or any of Tenant's fixtures or equipment or any alterations, improvements or decorations made by Tenant, or any Direct Tenant Work, (b) Landlord shall have no liability to Tenant for, and except as set forth in the next paragraph, Tenant shall not be entitled to terminate this Lease by virtue of, any delays in completion of repairs and (c) Landlord shall have the right to terminate this Lease upon giving written notice to Tenant at any time within thirty (30) days after the date of the damage if the Premises is damaged by fire or other casualty during the last six (6) months of the Term unless Tenant, having the right to renew the Term pursuant to an express provision contained in this Lease, has effectively extended the Term for a term in excess of one (1) year following the occurrence of the fire or other casualty.

(b) Tenant shall have the right to terminate this Lease by sending written notice of termination to Landlord within ninety (90) days after the Outside Date (as hereinafter defined) if the repair work is not completed by such date, subject to force majeure. "Outside Date" means (i) if the Landlord estimated that the repair work would require less than two hundred seventy (270) consecutive dates to complete, the 360th day after the date of such casualty or (ii) if Landlord estimated that the repair work would require more than two hundred seventy (270) consecutive days to complete, the date which is ninety (90) days after the estimated completion date set forth in the Repair Estimate.

12. **Landlord's Right to Enter**.

Tenant will permit Landlord, Landlord's agents or employees or any other person or persons authorized in writing by Landlord, upon at least twenty-four (24) hours prior notice (except in the event of an emergency):

(a) to inspect the Premises at any time,

(b) to enter the Premises if Landlord shall so elect for making alterations, improvements or repairs to the Building or for any purpose in connection with the operation or maintenance of the Building, and

(c) during the last twelve (12) months of the Term, to enter and exhibit the Premises to be let.

No such entry shall be treated as a deprivation or interference with Tenant's use and possession of the Premises; provided Landlord and its agents, employees or any other person or persons authorized in writing by the Landlord shall use commercially reasonable efforts to minimize interference with Tenant's use and occupancy of the Premises.

13. **Insurance**.

(a) Tenant will not do or commit any act or thing, or suffer or permit any act or thing to be done or committed, as a result of which any policy of insurance of any kind on or in connection with the Property shall become void or suspended, or the insurance risk on the Building or any other portion of the Property shall (in the opinion of the insuring companies) be rendered more hazardous. Tenant shall pay as additional rent the amount of any increase of premiums for such insurance, resulting from any breach of this covenant.

(b) Tenant shall maintain throughout the Term, at Tenant's expense:

(i) Commercial General Liability Insurance with coverage limits of not less than $1,000,000 combined single limit for bodily injury, personal injury, death and property damage per occurrence and per location aggregate insuring tenant and naming owner, landlord, partners, shareholders, members, officers, directors, mortgages, agents, representatives and employees (collectively landlord), including without limitation those parties set forth in subsection (c) below, as additional insureds insuring against any and all liability of the insureds with respect to the Premises or arising out of or related to any occurrences within the Premises, Tenant's use or occupancy of the Premises, the condition of the Premises, the acts or omissions of Tenant and its agents, employees, contractors in the Premises and elsewhere in the Building, the installation, construction and/or maintenance of the Tenant Improvements or other alterations or improvements by Tenant;

(ii) Workers' Compensation coverages required by law, together with Employers' Liability coverage with a limit of not less than $500,000 (or the statutory requirement if higher) per injury;

(iii) Property Insurance written on an ISO special causes of loss or similar form, covering the Tenant Improvements, all equipment, and contents in an amount of not less than the 100% replacement cost without co-insurance;

(iv) Insurance covering loss of income or business interruption losses for a period of one (1) year;

(v) Intentionally Omitted.

(vi) Automobile Liability Insurance including coverage for Hired Car and Non-Owned automobile liability with coverage limits of not less than $1,000,000 combined single limit for bodily injury and property damage; and

(vii) Umbrella Liability Insurance with coverage for the full limit carried by the Tenant but not less than $5,000,000 covering over the Commercial General Liability, and Employers' Liability limits outlined above. The Umbrella Liability limit should be sufficiently high to reflect the exposures presented.

(c) Landlord, Landlord's property manager, Landlord's asset manager and Landlord's mortgagees, shall be named as additional insured on a primary and non-contributory basis as respects General Liability outlined above.

(d) All insurance policies shall be issued by insurance carriers having an A.M. Best rating of A- VIII and licensed to do business in the state where the Building is located.

(e) Landlord shall maintain throughout the Term so-called all-risk or fire and extended coverage insurance upon the Building. The cost of the premiums for such insurance and of any endorsements thereto shall be deemed, for purposes of Article 4 of this Lease, to be part of the costs of operating and maintaining the Property. Landlord shall have the right, at its sole discretion to maintain other insurance as a reasonably prudent landlord would obtain for similar property.

(f) Notwithstanding anything in this Lease to the contrary, each party hereto hereby releases the other party, its agents and employees to the extent of the releasing party's actual recovery under its insurance policies, from any and all liability for any loss or damage which may be inflicted upon the property of such party, notwithstanding that such loss or damage shall have arisen out of the negligent act or omission of the other party, its agents or employees, provided, however, that this release shall be effective only with respect to loss or damage occurring during such times as the appropriate policy of insurance of the party so releasing shall contain a clause to the effect that such release shall not affect the said policy or the right of the insured to recover thereunder; each party hereto shall use reasonable efforts to have such a clause included in its said policies..

14. **Repairs and Condition of Premises**.

At the expiration or other termination of this Lease, Tenant shall leave the Premises, and during the Term will keep the same, in substantially the same order and condition as delivered to Tenant, ordinary wear and tear, damage by fire or other casualty (which fire or other casualty, to the extent the same only affects the Premises, has not occurred through the

negligence of Tenant or those claiming under Tenant or their employees or invitees respectively) and repairs to be performed by Landlord under Article 16(a)(v) of this Lease alone excepted; for that purpose and, except as stated in this Lease, Tenant will make all necessary repairs and replacements to the interior of the Premises, excluding any structural components of the Building. Tenant will use every reasonable precaution against fire and will give Landlord prompt notice of any damage to or accident upon the Premises. Tenant will also at all times, subject to Article 16(a)(iv) of this Lease, remove all dirt, rubbish, waste and refuse from the Premises and at the expiration or sooner termination of the Term will also have had removed all its property therefrom, to the end that Landlord may again have and repossess the Premises. Any of Tenant's property remaining on the Premises on the date of the expiration or termination of the Term shall be deemed abandoned by Tenant and may be removed and disposed of in such manner as Landlord may, at its sole discretion, determine, and Tenant shall reimburse Landlord, upon demand, for the cost of such removal and disposal, plus five percent (5%) for overhead.

15. **Compliance with Law**.

(a) Landlord shall be responsible for compliance with all laws and ordinances existing as of the Commencement Date and all notice requirements, orders, regulations and recommendations (whatsoever nature thereof may be) of any and all federal, state, county or municipal authorities, with respect to the Building, the Land, the common areas of the Building and the Land. Tenant shall comply promptly with all laws and ordinances, including, without limitation, the Americans With Disabilities Act, and all notices, requirements, orders,regulations and recommendations (whatever the nature thereof may be) of any and all the federal, state, county or municipal authorities or of the Board of Fire Underwriters or any insurance organizations, associations or companies, with respect to Tenant's use and occupancy of the Premises and any property appurtenant thereto and any use thereof; Tenant also agrees that it shall not knowingly do or commit any act or thing, or suffer to be done or committed any act or thing anywhere on the Property contrary to any of the laws, ordinances, notices, requirements, orders.

(b) "Environmental Laws" means all present or future federal, state or local laws, ordinances, rules or regulations (including the rules and regulations of the federal Environmental Protection Agency and comparable state agency) relating to the protection of human health or the environment. "Hazardous Materials" means pollutants, contaminants, toxic or hazardous wastes or other materials the removal of which is required or the use, treatment, storage or disposal of which is regulated, restricted, or prohibited by any Environmental Law.

(c) Tenant agrees that (i) no activity will be conducted on the Premises that will use or produce any Hazardous Materials, except for activities which are part of the ordinary course of Tenant's business, which may include chemistry and biology research and development activities (but which do not include the use or testing of live animals on the Premises) which are conducted in accordance with all applicable Environmental Laws ("Permitted Activities"); (ii) the Premises will not be used for storage of any Hazardous Materials, except for materials used in the Permitted Activities which are properly stored in a manner and location complying with all applicable Environmental Laws; (iii) no portion of the Premises or Property will be used by Tenant or Tenant's Agents for disposal of Hazardous Materials; (iv) promptly following Landlord's written request, Tenant will deliver to Landlord copies of all Material Safety Data Sheets and other written information prepared by

manufacturers, importers or suppliers of any chemical; and (v) Tenant will promptly notify Landlord of any violation by Tenant or Tenant's Agents of any Environmental Laws or the release or suspected release of Hazardous Materials in, under or about the Premises, and Tenant shall promptly deliver to Landlord a copy of any notice, filing or permit sent or received by Tenant with respect to the foregoing. If at any time during or after the Term, any portion of the Property is found to be contaminated by Tenant or Tenant's Agents or subject to conditions prohibited in this Lease caused by Tenant or Tenant's Agents, Tenant will indemnify, defend and hold Landlord harmless from all claims, demands, actions, liabilities, costs, expenses, reasonable attorneys' fees, damages and obligations of any nature arising from or as a result thereof, and Landlord shall have the right to direct remediation activities in coordination with Tenant and in compliance with all Laws, all of which shall be performed at Tenant's cost. Tenant's obligations pursuant to this subsection shall survive the expiration or termination of this Lease.

(d) Landlord hereby covenants and agrees that Landlord shall be responsible for all environmental remediation of the Property, if any, which is required from time to time by applicable Environmental Laws then in effect and applicable to the then current use of the Property, but only to the extent not caused or permitted by Tenant, its agents, servants, employees, contractors, invitees or subtenants. Tenant shall have no liability for any Hazardous Material located at the Property prior to the Commencement Date, or for any fines, penalties or other sanctions which may be imposed or asserted by any governmental entity having jurisdiction over the Property for any remediation activities for Hazardous Material located at the Property prior to the Commencement Date, including by reason of any failure to conduct such remediation activities or the failure to conduct such remediation activities in compliance with applicable law (collectively, "Environmental Costs").

16. **Services**.

(a) Landlord agrees that it shall:

(i) HVAC. Furnish heat, ventilation and air conditioning to the Premises, Monday through Friday from 8:00 AM to 6:00 PM, holidays excepted; holidays, as such term is used in this Lease, shall mean days observed as holidays by the United States government, the Commonwealth of Pennsylvania, the County of Chester or the Township of Tredyffrin, as well as days declared as holidays in any union contract affecting the operations of the Building; heat, ventilation and air conditioning required by Tenant at other times shall be supplied without additional charge, upon demand either through controls installed in the Premises or access to Landlord's building management system, it being understood that the heating, ventilating and air conditioning system serving the Premises shall be available to Tenant on a 24 hour per day, 7 day per week basis, without charge other than Tenant Energy Costs. The heating, ventilating, and air conditioning shall provide reasonably comfortable conditions, provided that in any given room or area of Tenant's demised premises, the occupancy does not exceed one person for each 150 square feet, and total electric load does not exceed 5 watts per sq. ft. (plus supplemental power added by Tenant, if required) for all purposes, including lighting and power; Landlord shall not be responsible for the failure of the air conditioning system to meet the foregoing design performance specifications if such failure results from excess occupancy of the Premises or if Tenant installs and operates machines and appliances, the installed electrical load of which, when combined with the load of all lighting fixtures, exceeds 5 watts per sq. ft.; if the Premises are used in a manner exceeding the aforementioned occupancy

and electric load criteria, Tenant shall pay to Landlord, promptly upon billing, Landlord's costs of supplying air conditioning resulting from such excess, (without markup) as reasonably determined by Landlord; if due to use of the Premises in a manner exceeding the aforementioned occupancy and electrical load criteria, or due to rearrangement of partitioning after the initial preparation of the Premises, interference with normal operation of the heating, ventilating or air conditioning in the Premises results, necessitating changes in the system servicing the Premises, such changes may be made by Landlord upon request by Tenant at Tenant's sole cost and expense, subject to the provisions of section (b) of this Article 16. Tenant agrees at all times to cooperate fully with Landlord and to abide by all of the regulations and requirements which Landlord may reasonably prescribe for the proper functioning and protection of the said heating, ventilating and air conditioning system; the foregoing heating, ventilating and air conditioning services shall be subject to any statute, ordinance, rule, regulation, resolution or recommendation for energy conservation which may be promulgated by any governmental agency or organization and which Landlord in good faith may elect to abide by or shall be required to abide by. On the Commencement Date, Landlord shall deliver all heat pumps and HVAC units (the "HVAC Equipment") servicing the Premises in good working order and condition. Notwithstanding the foregoing or anything to the contrary contained herein, Tenant shall be solely responsible at its sole cost and expense, for the maintenance and repair of the HVAC Equipment and any supplemental heat, ventilation and air conditioning unit in the Premises whether installed by Tenant or in the Premises on the Commencement Date. The cost of replacement of any HVAC Equipment shall be paid by Landlord without pass through to Tenant as an Operating Expense;

(ii) Elevators. Provide passenger elevator service to the Premises during all working days (Saturday, Sunday and holidays excepted) from 8:00 AM to 6:00 PM, with one (1) elevator subject to call at all other times;

(iii) Access. Furnish to Tenant's employees and agents access to the Premises at all times, subject to compliance with such reasonable security measures as shall be in effect for the Building;

(iv) Janitorial. Provide to the Premises janitorial service in accordance with the schedule annexed hereto as **Exhibit "F"**; any and all additional or specialized janitorial service desired by Tenant shall be contracted for by Tenant directly with Landlord's janitorial agent and the cost and payment thereof shall be and remain the sole responsibility of Tenant; no trash removal services will be provided by Landlord for the removal of trash or refuse of a character or quantity not customary for normal office users, unless Tenant shall first agree to the payment of Landlord's cost thereof;

(v) Repairs. Make all structural repairs to the Building and the Premises, all repairs which may be needed to the mechanical, HVAC, electrical and plumbing systems in and/or servicing the Premises (excluding repairs to any non-building standard fixtures, supplemental HVAC units and equipment, and/or other improvements installed or made by or at the request of Tenant all of which must be repaired and maintained by the Tenant), and all repairs to exterior windows and glass (including caulking and weatherstripping); in the event that any repair is required by reason of the negligence or abuse of Tenant or its agents, employees, invitees or of any other person using the Premises with Tenant's consent, express or implied, Landlord may make such repair and the cost thereof, plus ten percent (10%) of such cost for Landlord's overhead, shall be paid by Tenant to Landlord within fifteen (15) days after

demand, unless Landlord shall have actually recovered or has the right to recover such cost through insurance proceeds;

(vi) Water. Provide hot and cold water, for drinking, lavatory, toilet and ordinary cleaning purposes, at each floor;

(vii) Public Areas. Keep and maintain the public areas and facilities of the Building clean and in good working order, and the sidewalks and parking areas adjoining the Building in good repair and free and clear from accumulations of snow, ice and debris;

(viii) Electricity. Furnish to Tenant electric energy as required by Tenant but in no event exceeding 5 watts per square foot of rentable area for the use of Tenant in the Premises; Landlord shall install and maintain such meters as Landlord shall deem necessary to measure, respectively, the consumption by Tenant and each other tenant of the Building of electric energy in the respective areas of the Building leased to tenants; Landlord shall not be liable in any way to Tenant for failure or defect in the supply or character of electric energy furnished to the Premises or to the Building by reason of any requirement, act or omission of the public utility serving the Building with electricity or for any other reason whatsoever not attributable to Landlord; Tenant agrees, to the extent, if any, in the future required by the Pennsylvania Public Utility Commission or federal or state law as a necessary condition to the supply of electric energy to the Premises, to become an individually metered customer of such public utility, in which event, upon receipt of each bill to Tenant from such public utility for electric service to the Premises, Tenant shall pay directly to the public utility company the amount of such bill; Landlord shall furnish and install all replacement tubes, lamps, bulbs and ballasts required in the Premises, at Tenant's expense; Tenant's use of electric energy in the Premises shall not at any time exceed the capacity of any of the electrical conductors and equipment in or otherwise serving the Premises.

(ix) Signage. Landlord shall provide Tenant with building standard directory and suite entrance signage at Landlord's cost. Any modifications to such signage shall be subject to the prior approval of Landlord and Tenant shall be required to pay all costs related to any such modification. Provided that Tenant occupies no less than 40,000 rentable square feet within the Building, Tenant shall also be permitted, subject to Landlord's approval (not to be unreasonably withheld, conditioned or delayed), to install signage on fifty percent (50%) of the existing monument located at the Building. In the event that Tenant desires to install any graphics/furniture/decorations on the second floor outside of the Premises, or inside the Premises that are visible from outside of the Premises, such graphics shall be approved in writing by the Landlord prior to installation, such consent not to be unreasonably withheld, conditioned or delayed.

(b) Special Equipment. Other than as installed as part of the Tenant Improvements, Tenant shall not install any equipment of any kind or nature whatsoever which would or might necessitate any changes, replacements or additions to any of the heating, ventilating, air conditioning, electric, sanitary, elevator or other systems serving the Premises or any other portion of the Building; or to any of the services required of Landlord under this Lease, without the prior written consent of the Landlord (which consent shall not be unreasonably withheld, conditioned or delayed). In the event that such consent is granted, such replacements, changes or additions shall be paid for by Tenant. At the expiration or earlier termination of the

Term, Tenant shall pay to Landlord Landlord's cost of restoring such systems (other than those installed as components of the Tenant Improvements) to their condition prior to such replacements, changes or additions, unless Landlord has required such special equipment to be removed.

(c) Interruption of Service. In case of accident, strikes, inability to obtain supplies, breakdowns, repairs, renewals or improvements to the Building or replacement of machinery therein, or for other cause pertaining to the Building deemed reasonably sufficient by Landlord in its reasonable judgment, the operation of any of the elevators or other machinery or apparatus may be changed or suspended; provided Landlord shall use reasonable efforts to minimize interference with Tenant's use and occupancy in connection therewith. As to heat, ventilation, air conditioning, cleaning service, electricity and elevator service, and any other services, Landlord shall not be responsible or liable in any way for any failure, interruption or inadequacy in the quantity or quality of the same where directly caused by war, civil commotion, governmental restrictions, prohibitions or other regulations, strikes, labor disturbances, inability to obtain adequate supplies or materials, casualties, repairs, replacements, or causes beyond Landlord's reasonable control whether similar or dissimilar to the foregoing, provided that Landlord shall use commercially reasonable efforts to mitigate any such failure, interruption or inadequacy. Notwithstanding the foregoing, however, if a cessation of the elevator or other mechanical apparatus, electric, heating, ventilation or air conditioning service occurs which (i) materially impairs the ability of Tenant to access or utilize all or a substantial portion of the Premises due to such condition, (ii) was caused by, or continues due to, the negligence or willful misconduct of Landlord or Landlord's agents or employees, and (iii) continues for more than five (5) business days, then Fixed Rent shall abate beginning on the sixth (6th) business day and shall continue until service is fully restored.

17. **Notice of Breakage, Fire, Theft**.

Tenant shall give to Landlord prompt written notice, but in no event later than forty-eight (48) hours after obtaining knowledge of the occurrence in question, of any

(a) accident or breakage or defects in the window glass, wires, plumbing or heating ventilating or cooling apparatus, elevators or other apparatus, walls or ceiling tiles affecting the Premises,

(b) fire or other casualty affecting the Premises, or

(c) theft affecting the Premises.

18. **Indemnification; Release**.

(a) Subject to Article 13(f), Landlord shall not be held responsible for and is hereby expressly relieved from any and all liability by reason of any injury, loss, or damage to any person or property in or about the Premises or the Property whether the loss, injury or damage be to the person or property of Tenant or any other person, unless due to the negligence or willful misconduct of Landlord or its agents, employees or contractors. Subject to Article 13(f), Tenant agrees further to indemnify, defend and save Landlord harmless from and against all claims, actions, damages, liabilities and expenses, including but not limited to reasonable

attorneys' fees and other legal expenses, on account of such injury, loss or damage arising (i) from any occurrence in, upon or at the Premises, unless due to the negligence or willful misconduct of Landlord, or Landlord's agents, contractors, invitees and employees, or (ii) from any occurrence in or about the Property arising from the negligence or willful misconduct of Tenant.

(b) Tenant shall not be held responsible for and is hereby expressly relieved from any and all liability by reason of any injury, loss, or damage to any person or property in or about the Property (exclusive of the Premises) whether the loss, injury or damage be to the person or property of Landlord or any other person, unless due to the negligence or willful misconduct of Tenant. Landlord agrees to indemnify, defend and save Tenant harmless from and against all claims, actions, damages, liabilities and expenses, including but not limited to reasonable attorneys' fees and other legal expenses, on account of such injury, loss or damage arising from (i) the negligence or willful misconduct of Landlord and Landlord's agents, contractors, invitees and employees, and (ii) any breach, violation, or non-performance by Landlord of any term, covenant, or provision of this Lease.

19. **Mechanics' and Other Liens**.

(a) Tenant covenants that it shall not (and has no authority to) create or allow any encumbrance against the Premises, the Property, the Building or any part of any of them or Landlord's interest therein.

(b) Tenant covenants that it shall not suffer or permit to be created, or to remain, any lien or claim thereof (arising out of any work done or services, material, equipment or supplies furnished for or at the request of Tenant or by or for any contractor or subcontractor of Tenant), but not to the extent resulting from the acts or omissions of Landlord or Landlord's agents, contractors or employees, which is or may become a lien upon the Premises, the Property, the Building or any part of any of them or the income therefrom or any fixture, equipment or similar property therein.

(c) If any lien or claim shall be filed, Tenant, within twenty (20) days after obtaining actual notice of the filing thereof, shall cause the same to be discharged of record by payment, deposit, bond or otherwise. If Tenant shall fail to cause such lien or claim to be discharged and removed from record within that period, then, without obligation to investigate the validity thereof and in addition to any other right or remedy Landlord may have, Landlord may, but shall not be obligated to, contest the lien or claim or discharge it by payment, deposit, bond or otherwise; and Landlord shall be entitled, if Landlord so decides, to compel the prosecution of an action for the foreclosure of such lien by the lienor and to pay the amount of the judgment in favor of the lienor with interest and costs. Any amounts so paid by Landlord and all costs and expenses, including attorneys' fees, incurred by Landlord in connection therewith, together with interest at the Lease Interest Rate from the respective dates of Landlord's making of the payment or incurring of the cost or expense, shall constitute additional rent payable by Tenant under this Lease and shall be paid by Tenant to Landlord within twenty (20 days after Tenant's receipt of written demand therefor.

(d) Notwithstanding anything to the contrary in this Lease or in any other writing signed by Landlord, neither this Lease nor any other writing signed by Landlord shall be

construed as evidencing, indicating, or causing an appearance that any erection, construction, alteration or repair to be done, or caused to be done, by Tenant is or was in fact for the immediate use and benefit of Landlord. Further, notwithstanding anything contained herein to the contrary, nothing contained in or contemplated by this Lease shall be deemed or construed in any way to constitute the consent or request on the part of Landlord for the performance of any work or services or the furnishing of any materials for which any lien could be filed against the Premises or the Building or the Property or any part of any of them, nor as giving Tenant any right, power, or authority to contract for or permit the performance of any work or services or the furnishing of any materials for which any lien could be filed against the Premises, the Building, the Property or any part of any of them.

(e) Promptly after the completion of any work or the delivery of any material to the Premises by any contractor, subcontractor or materialman engaged by Tenant, Tenant shall deliver to the Landlord partial and/or final releases of liens (whichever shall be applicable) from each such contractor, subcontractor or materialman for work that has been performed and paid for to date and, upon completion of any project, an affidavit from its contractor that it and all subcontractors and materialmen hired by it have been paid for all work done with respect to the project. With respect to any project that is bonded, prior to the commencement of any work Tenant shall also provide Landlord with a copy of a Waiver of Liens from its contractor which has been filed with the Prothonotary of Chester County, Pennsylvania.

20. **Default by Landlord**.

Landlord shall be in default of this Lease if it fails or refuses to perform any provision of this Lease that it is obligated to perform if the failure to perform is not cured within thirty (30) days (or such shorter period of time as reasonably required by Tenant in an emergency situation) after notice of the default has been given by Tenant to Landlord. If the non-monetary default cannot reasonably be cured within thirty (30) days, Landlord shall not be in default of this Lease if Landlord commences to cure the default within the thirty (30) day period and diligently and in good faith continues to cure the default. Upon any such default by Landlord under this Lease, Tenant may, except as otherwise specifically provided in this Lease to the contrary, exercise any of its rights provided at law or in equity. Any final unappealable award from a court or arbitrator in favor of Tenant requiring payment by Landlord which is not paid by Landlord within the time period directed by such award, may be offset by Tenant from Fixed Rent next due and payable under this Lease; provided, however, Tenant may not deduct the amount of the award against more than fifty percent (50%) of Fixed Rent next due and owing (until such time as the entire amount of such judgment is deducted).

21. **Defaults - Remedies**.

If any of the following (each, an "Event of Default") shall occur:

(a) Tenant does not pay in full within five (5) business days written notice (provided that such notice shall not be required more than two (2) times in any twelve (12) month period) when due any and all installments of rent (whether Fixed Rent or additional rent) or any other charge or payment whether or not herein included as rent;

(b) Tenant violates or fails to perform or comply with any non-monetary covenant, agreement or condition herein contained, and such failure is not cured within thirty (30) days after notice from Landlord; provided however, if Tenant's failure to comply cannot reasonably be cured within thirty (30) days, Tenant shall be allowed additional time (not to exceed ninety (90) additional days) as is reasonably necessary to cure the failure so long as Tenant begins the cure within thirty (30) days and diligently pursues the cure to completion;

(c) Intentionally omitted; or

(d) An involuntary case under the federal bankruptcy law as now or hereafter constituted is commenced against Tenant or any guarantor or surety of Tenant's obligations under this Lease ("Guarantor"), or under any other applicable federal or state bankruptcy, insolvency, reorganization, or other similar law, or there is filed against Tenant or a Guarantor a petition seeking the appointment of a receiver, liquidator or assignee, custodian, trustee, sequestrator (or similar official) of Tenant or a Guarantor of any substantial part of Tenant's or a Guarantor's property, or seeking the winding-up or liquidation of Tenant's or a Guarantor's affairs and such involuntary case or petition is not dismissed within ninety (90) days after the filing thereof, of if Tenant or a Guarantor commences a voluntary case or institutes proceedings to be adjudicated as bankrupt or insolvent or consents to the entry of an order for relief under the federal bankruptcy laws as now or hereafter constituted, or any other applicable federal or state bankruptcy or insolvency or other similar law, or consents to the appointment of or taking possession by a receiver or liquidator or assignee, trustee, custodian, sequestrator (or other similar official) of Tenant or a Guarantor of any substantial part of Tenant's or a Guarantor's property, or if Tenant or any Guarantor makes any assignment for the benefit of creditors or admits in writing its inability to pay its debts generally as they become due or if Tenant is levied upon and is about to be sold out upon the Premises by any sheriff, marshal or constable, or if Tenant or any Guarantor is a corporation and is dissolved or liquidated,

Then, and in any such event, at the sole option of Landlord,

(i) The whole balance of rent and all other sums payable hereunder for the entire balance of the term of this Lease, herein reserved or agreed to be paid by Tenant, or any part of such rent, charges and other sums, discounted to present value at a rate of six percent (6%) shall be taken to be due and payable from Tenant and in arrears as if by the terms of this Lease said balance of rent, charges and other sums and expenses were on that date payable in advance; and/or

(ii) Landlord may terminate this Lease by written notice to Tenant. If Landlord elects to terminate this Lease, Landlord, in addition to Landlord's other remedies, may recover from Tenant a judgment for damages equal to the sum of the following:

(A) the unpaid rent and other sums which became due up to the time of such termination plus interest from the dates such rent and other sums were due to the date of the judgment at the Lease Interest Rate; plus

(B) the present value at the time of judgment of the amount by which the unpaid rent and other sums which would have become due (had this Lease not been

terminated) after termination until the date of the judgment exceeds the amount of loss of such rental and other sums Tenant proves could have been reasonably avoided; plus

(C) the amount (as discounted at the rate of four percent (4%) per annum) by which the unpaid rent and other sums which would have become due (had this Lease not been terminated) for the balance of the term after the date of judgment exceeds the amount of loss of such rental and other sums that Tenant proves could have been reasonably avoided; plus

(D) any other amount necessary to compensate Landlord for all the detriment proximately caused by Tenant's failure to perform its obligations under this Lease or which in the ordinary course would be likely to result therefrom including, without limitation, the cost of repairing the Premises and reasonable attorneys' fees; plus

(E) at Landlord's election, such other amounts in addition to or in lieu of the foregoing as may be permitted by applicable law.

As used in the foregoing clause (B), the "present value at the time of judgment" shall be computed by adding to the rent past due or which would have become due interest at the Lease Interest Rate from the dates such rent was or would have become due to the date of the judgment; and/or

(iii) Landlord may terminate Tenant's right of possession and may reenter and repossess the Premises by legal proceedings, force or otherwise, as allowed by law, without terminating this Lease. After reentry or retaking or recovering of the Premises, whether by termination of this Lease or not, Landlord may, but shall be under no obligation to, make such alterations and repairs, as Landlord may deem then necessary or advisable to relet the Premises or any part or parts thereof, either in Landlord's name or otherwise, for a term or terms which may at Landlord's option be less than or exceed the period which otherwise would have constituted the balance of the term of this Lease and at such rent or rents and upon such other terms and conditions as in Landlord's sole discretion may seem advisable and to such person or persons as may in Landlord's sole discretion seem best; and whether or not the Premises are relet, Tenant shall be liable for any loss, for such period as is or would have been the balance of the term of this Lease, of rent and all other sums payable under this Lease, plus the reasonable and actual costs and expenses of reletting and of redecorating, remodeling or making repairs and alterations to the Premises for the purpose or reletting, the amount of such liability to be computed monthly and to be paid by Tenant to Landlord from time to time upon demand. Landlord shall in no event be liable for, nor shall any damages or other sums to be paid by Tenant to Landlord be reduced by, failure to relet the Premises or failure to collect the rent or other sums from any reletting. Tenant shall not be entitled to any rents or other sums received by Landlord in excess of those provided for in this Lease. Tenant agrees that Landlord may file suit to recover any rent and other sums falling due under the terms of this Article from time to time and that no suit or recovery of any amount due hereunder to Landlord shall be any defense to any subsequent action brought for any other amount due hereunder to Landlord. Tenant, for Tenant and Tenant's successors and assigns, after Landlord's delivery to Tenant of written notice of default and the passing of any applicable cure periods, hereby irrevocably constitutes and appoints Landlord, Tenant's and their agent to collect the rents due or to become due under all subleases of the Premises or any parts thereof and Landlord shall apply such rents to Tenant's

unpaid rental obligations under this Lease. Notwithstanding any reletting without termination, Landlord may at any time thereafter elect to terminate this Lease for Tenant's previous Event of Default.

Whenever Landlord shall have the right to reenter the Premises under this Lease, it shall have the right to remove all persons and property from the Premises and either treat such property as abandoned or at Landlord's option store it in a public warehouse or elsewhere at the cost of and for the account of Tenant, all without service of notice or resort to legal process and without being deemed guilty of trespass, or becoming liable for any loss or damage which may be occasioned thereby.

Tenant waives the right to any notice to remove as may be specified in the Landlord and Tenant Act of Pennsylvania, Act of April 6, 1951, as amended, or any similar or successor provision of law.

For the purposes of computing "the whole balance of rent and all other sums payable hereunder for the entire balance of the term of this Lease," "the unpaid rent and other sums which would have become due (had this Lease not been terminated) after termination until the date of the judgment" and "the unpaid rent and other sums which would have become due (had this Lease not been terminated) for the balance of the term after the date of judgment," as such quoted or any similar phrases are used in this Article 21, the amounts of additional rents which would have been due per year under this Lease shall be such amounts as Landlord shall reasonably estimate to be the per annum rates of additional rent for the calendar year during which this Lease was terminated or during which rent was accelerated, increasing annually on the first day of each calendar year thereafter at the rate of six percent (6%) per annum compounded.

The parties recognize that no adequate remedy at law may exist for a breach of Articles 6, 7 and 10 hereof. Accordingly, Landlord may obtain specific performance of any provision of Articles 6, 7 and 10 hereof. Neither such right nor its exercise shall limit any other remedies which Landlord may have against Tenant for a breach of such Articles, including, without limitation, all remedies available under this Article 21. The reference herein to specific performance in connection with Articles 6, 7 and 10 shall not preclude the availability of specific performance, in any appropriate case, for the breach or threatened breach of any other provision of this Lease.

In addition to other remedies available to Landlord herein, Landlord may (but shall not be obligated to do so), cure any uncured Event of Default on behalf of Tenant, and Tenant shall reimburse Landlord within thirty (30) days of receipt of written demand for all reasonable costs actually incurred by Landlord in curing such default, including, without limitation, reasonable attorneys' fees and other legal expenses, together with interest thereon at the Lease Interest Rate, which costs and interest thereon shall be deemed additional rent hereunder.

Also in addition to, and not in lieu of any of the foregoing rights granted to Landlord:

(A) INTENTIONALLY OMITTED.

(B) WHEN THIS LEASE OR TENANT'S RIGHT OF POSSESSION SHALL BE TERMINATED UPON AN EVENT OF DEFAULT OR FOR ANY OTHER REASON, EITHER DURING THE TERM OF THIS LEASE, AND ALSO WHEN AND AS SOON AS SUCH TERM SHALL HAVE EXPIRED OR BEEN TERMINATED, TENANT HEREBY IRREVOCABLY AUTHORIZES AND EMPOWERS ANY ATTORNEY OR ANY COURT OF RECORD AS ATTORNEY FOR TENANT AND ANY PERSONS CLAIMING THROUGH OR UNDER TENANT TO CONFESS JUDGMENT IN EJECTMENT AGAINST TENANT AND ALL PERSONS CLAIMING THROUGH OR UNDER TENANT FOR THE RECOVERY BY LANDLORD OF POSSESSION OF THE PREMISES, FOR WHICH THIS LEASE SHALL BE SUFFICIENT WARRANT, WHEREUPON, IF LANDLORD SO DESIRES, A WRIT OF EXECUTION OR OF POSSESSION MAY ISSUE FORTHWITH, WITHOUT ANY PRIOR WRIT OR PROCEEDINGS WHATSOEVER, AND PROVIDED THAT IF FOR ANY REASON AFTER SUCH ACTION SHALL HAVE BEEN COMMENCED THE SAME SHALL BE DETERMINED, CANCELED OR SUSPENDED AND POSSESSION OF THE PREMISES HEREBY DEMISED REMAIN IN OR BE RESTORED TO TENANT OR ANY PERSON CLAIMING THROUGH OR UNDER TENANT, LANDLORD SHALL HAVE THE RIGHT, UPON ANY SUBSEQUENT EVENT OF DEFAULT OR EVENTS OF DEFAULT, OR UPON ANY SUBSEQUENT TERMINATION OR EXPIRATION OF THIS LEASE OR ANY RENEWAL OR EXTENSION HEREOF, OR OF TENANT'S RIGHT OF POSSESSION, AS HEREINBEFORE SET FORTH, TO CONFESS JUDGMENT IN EJECTMENT AS HEREINBEFORE SET FORTH ONE OR MORE ADDITIONAL TIMES TO RECOVER POSSESSION OF THE SAID PREMISES.

IN ANY ACTION OF OR FOR EJECTMENT, IF LANDLORD SHALL FIRST CAUSE TO BE FILED IN SUCH ACTION AN AFFIDAVIT MADE BY IT OR SOMEONE ACTING FOR IT SETTING FORTH THE FACTS NECESSARY TO AUTHORIZE THE ENTRY OF JUDGMENT, SUCH AFFIDAVIT SHALL BE CONCLUSIVE EVIDENCE OF SUCH FACT; AND IF A TRUE COPY OF THIS LEASE (AND OF THE TRUTH OF THE COPY SUCH AFFIDAVIT SHALL BE SUFFICIENT EVIDENCE) BE FILED IN SUCH ACTION, IT SHALL NOT BE NECESSARY TO FILE THE ORIGINAL AS A WARRANT OF ATTORNEY, ANY RULE OF COURT, CUSTOM OR PRACTICE TO THE CONTRARY NOTWITHSTANDING. TENANT RELEASES TO LANDLORD, AND TO ANY AND ALL ATTORNEYS WHO MAY APPEAR FOR TENANT, ALL PROCEDURAL ERRORS IN ANY PROCEEDINGS TAKEN BY LANDLORD, WHETHER BY VIRTUE OF THE WARRANTS OF ATTORNEY CONTAINED IN THIS LEASE OR NOT, AND ALL LIABILITY THEREFOR, PROVIDED, HOWEVER, NOTHING CONTAINED HEREIN SHALL BE CONSTRUED TO PREVENT TENANT FROM FILING A PETITION TO OPEN OR STRIKE ANY JUDGMENT.

As used in this Article 21, the "term" shall include the Term of this Lease and any renewals or extensions thereof to which Tenant shall have become bound.

22. **Remedies Cumulative**.

All remedies available to Landlord under this Lease and at law and in equity shall be cumulative and concurrent. No termination of this Lease or taking or recovering possession of the Premises shall deprive Landlord of any remedies or actions against Tenant for rent, for

charges or for damages for the breach of any covenant or condition herein contained, nor shall the bringing of any such action for rent, charges or breach of covenant or condition, nor the resort to any other remedy or right for the recovery of rent, charges or demands for such breach be construed as a waiver or release of the right to insist upon the forfeiture and to obtain possession. No reentering or taking possession of the Premises, or making of repairs, alterations or improvements thereto, or reletting thereof, shall be construed as an election on the part of Landlord to terminate this Lease unless written notice of such intention be given by Landlord to Tenant. The failure of Landlord to insist upon strict and/or prompt performance of the terms, agreements, covenants and conditions of this Lease or any of them, and/or the acceptance of such performance thereafter shall not constitute or be construed as a waiver of Landlord's right to thereafter enforce the same strictly according to the tenor thereof in the event of a continuing or subsequent default.

23. **Excepted from Premises**.

In the event that **Exhibit "A"** shows as being within the Premises, hallways, passageways, stairways, elevators, or other means of access to and from the Premises or the upper and lower portions of the Building, the space occupied by the said hallways, passageways, stairways, elevators and other means of access, although within the Premises as described hereinabove, shall be taken to be excepted therefrom and reserved to Landlord or to the other lessees of the Building and the same shall not be considered a portion of the Premises. All ducts, pipes, wires or other equipment used in the operation of the Building, or any part thereof, and any space occupied thereby, whether or not within the Premises as described hereinabove, shall likewise be excepted and reserved from the Premises, and Tenant shall not remove or tamper with or use the same and will permit Landlord to enter the Premises to service, replace, remove or repair the same.

24. **Lease Subordinated**.

(a) Subject to receipt of the required subordination, non-disturbance and attornment agreement, as provided below, this Lease shall be subject and subordinate at all times to the lien of any mortgage, deed of trust, ground lease, installment sale agreement and/or other instrument or encumbrance hereafter placed upon any or all of Landlord's interest or estate in the Premises or the remainder of the Property and of all renewals, modifications, consolidations, replacements and extensions thereof (all of which are hereinafter referred to collectively as a "mortgage"). The Tenant shall, at the request of the holder of any such mortgage, attorn to such holder, and shall execute, enseal, acknowledge and deliver, upon demand by the Landlord or such holder, such further instrument or instruments evidencing such subordination of the Tenant's right, title and interest under this Lease to the lien of any such mortgage, and such further instrument or instruments evidencing and elaborating such attornment, as shall be reasonably desired by such holder. Notwithstanding the foregoing, as a condition to Tenant's agreement to subordinate this Lease, Landlord, at Tenant's expense, shall use commercially reasonable efforts to obtain a subordination, non-disturbance and attornment agreement any future mortgage holders, within thirty (30) of any new mortgage on the Property. Landlord represents and warrants that there are no mortgages, deeds of trust, ground leases, installment sale agreements and/or other instruments or encumbrances placed upon any or all of Landlord's interest or estate in the Premises or the remainder of the Property as of the execution date of this Lease.

(b) Anything contained in the foregoing provisions of this Article to the contrary notwithstanding, any such holder may at any time subordinate its mortgage to the operation and effect of this Lease, without the necessity of obtaining the Tenant's consent thereto, by giving notice of the same in writing to the Tenant, and thereupon this Lease shall be deemed to be prior to such mortgage without regard to their respective dates of execution, delivery and/or recordation, and in that event such holder shall have the same rights with respect to this Lease as though this Lease shall have been executed, delivered and recorded prior to the execution and delivery of such mortgage.

25. **Condemnation**.

(a) If the whole or a substantial part of the Building shall be taken or condemned for a public or quasi-public use under any statute or by right of eminent domain or private purchase in lieu thereof by any competent authority, Tenant shall have no claim against Landlord and shall not have any claim or right to any portion of the amount that may be awarded as damages or paid as a result of any such condemnation or purchase including, without limit, any right of Tenant to damages for loss of its leasehold; all right of Tenant to damages therefor are hereby assigned by Tenant to Landlord. The foregoing shall not, however, deprive Tenant of any separate award for moving expenses, business dislocation damages or for any other award which would not reduce the award payable to Landlord. Upon the date the right to possession shall vest in the condemning authority, this Lease shall cease and terminate with rent adjusted to such date and Tenant shall have no claim against Landlord for the value of any unexpired term of this Lease.

(b) In the event of any temporary eminent domain taking of the Premises or any part thereof for temporary use, this Lease shall not be affected in any manner, the Term shall not be reduced, and the Tenant shall continue to pay in full the Fixed Rent, additional rent and all other sums of money and charges in this Lease reserved and provided to be paid by Tenant and Tenant shall be entitled to receive for itself such portion of any eminent domain award made for such temporary use with respect to the period of the taking which is within the Term; provided that if such temporary taking shall remain in full force at the expiration or earlier termination of this Lease, the award shall be apportioned between Landlord and Tenant in proportion to the respective portions of the period of temporary taking which falls within the Term and which falls outside the Term.

26. **Force Majeure**.

For purposes of this Lease, the term "force majeure" shall mean any delay or stoppage of the work or obligations under the Lease (except the payment of money) to the extent caused solely by strikes, lockouts, labor disputes not caused by the party claiming force majeure, acts of God, acts of war, terrorist acts, governmental actions, civil commotions, fire or other casualty, and other causes beyond the reasonable control of the party obligated to perform (collectively, a "force majeure"), and such force majeure shall excuse the performance of such party for a period equal to any such prevention, delay or stoppage and the time period for performance of the party's obligations shall be extended by the period of any delay in such party's performance caused by a force majeure. The party claiming force majeure shall provide notice thereof to the other party within 72 hours of such an event.

27. **Notices**.

(a) Each notice, demand, request or other communication required or permitted under the terms of this Lease shall be in writing and, unless and until otherwise specified in a written notice by the party to receive it, shall be sent to the parties at the following respective addresses:

If intended for Tenant prior to Commencement Date:

Trevena, Inc.
1018 W. 8th Avenue, Suite A
King of Prussia, PA 19406
Attention: General Counsel

If intended for Tenant after Commencement Date:

Trevena, Inc.
955 Chesterbrook Boulevard, Suite 200
Wayne, PA 19087
Attention: General Counsel

If intended for Landlord:

Chesterbrook Partners, LP
955 Chesterbrook Boulevard, Suite 120
Wayne, PA 19087-5615
Attention: Property Manager

with a copy to:

Chesterbrook Partners, LP
41 University Drive, Suite 206
Newtown, PA 18940
Attention: Director of Property Management

with a copy to:

Saul Ewing LLP
1200 Liberty Ridge Drive, Suite 200
Wayne, PA 19087
Attention: Michael S. Burg, Esquire

Notices may be given on behalf of any party by its legal counsel.

(b) Each such notice, demand, request or other communication shall be deemed to have been properly given for all purposes if (i) hand delivered, or (ii) mailed by registered or certified mail of the United States Postal Service, return receipt requested, postage

prepaid, or (iii) delivered to a nationally recognized overnight courier service for next business day (or sooner) delivery, or

(c) Each such notice, demand, request or other communication shall be deemed to have been received by its addressee, and to have been effectively given, upon the earlier of (i) actual delivery, (ii) refusal of acceptance at the proper address, or (iii) three (3) business days after deposit thereof at any main or branch United States post office, if sent, in accordance with clause (ii) of subsection (b) of this Article and (iv) one (1) business day after delivery to the courier, if sent pursuant to clause (iii) of subsection (b) of this Article.

28. **Definition of "the Landlord"**.

The word "Landlord" is used herein to include the Landlord named above and any subsequent owner of such Landlord's interest in the Building in which the Premises are located, as well as their respective heirs, personal representatives, successors and assigns, each of whom shall have the same rights, remedies, powers, authorities, obligations, liabilities, and privileges as it would have had had it originally signed this Lease as Landlord, including the right to proceed in its own name to enter judgment by confession or otherwise, but any such person, whether or not named herein, shall have no liability hereunder after it ceases to hold such interest. Neither Landlord nor any principal of or partner in Landlord, whether disclosed or undisclosed, shall be under any personal liability with respect to any of the provisions of this Lease and if Landlord shall default in the performance of Landlord's obligations under this Lease or otherwise, Tenant shall look solely to the equity of Landlord in its interest in the Property for the satisfaction of Tenant's remedies. It is expressly understood and agreed that Landlord's liability under the terms, covenants, conditions, warranties and obligations of this Lease shall in no event exceed the loss of Landlord's equity in its interest in the Property.

29. **Definition of "the Tenant"**.

As used herein, the term "Tenant" shall be deemed to refer to each and every person and/or entity hereinabove named as such and to such persons' and/or entities' respective heirs, personal representatives, successors and assigns, each of whom shall have the same rights, remedies, powers, authorities, obligations, liabilities, and privileges as it would have possessed had it originally executed this Lease as the Tenant. However, no such rights, remedies, powers, authorities, obligations, liabilities, and privileges shall inure to the benefit of any assignee of the Tenant, immediate or remote, unless, (a) pursuant to a Permitted Transfer, (b) the assignment to such assignee has been approved in writing by Landlord if required by the provisions of this Lease and such assignee shall have executed and delivered to Landlord the written documents that may be required by Landlord referred to hereinbefore, or (c) Landlord has consented to a sale of all of the assets of Tenant. Each and every person hereinabove named as the Tenant shall be bound jointly and severally by the terms, covenants and agreements contained herein.

30. **Estoppel Certificate; Mortgagee Lease Comments**.

(a) Both parties agree that from time to time, within ten (10) business days after a written response from the other party to, execute, enseal, acknowledge and deliver to the requesting party a written instrument in recordable form.

(i) certifying that

(A) this Lease is in full force and effect and has not been modified, supplemented or amended in any way (or, if there have been modifications, supplements or amendments thereto, that it is in full force and effect as modified, supplemented or amended and stating such modifications, supplements and amendments) and that the Lease (as modified, supplemented or amended, as aforesaid) represents the entire agreement among Landlord and Tenant as to the Premises and the leasehold;

(B) the dates to which the Fixed Rent, additional rent and other charges arising under this Lease have been paid, if any;

(C) the amount of any prepaid rents or credits due to Tenant, if any; and

(D) if applicable, Tenant has accepted the possession of the Premises and has entered into occupancy of the Premises and the date on which the Term shall have commenced and the corresponding expiration date;

(ii) stating whether or not to the best knowledge of the signer of such certificate all conditions under the Lease to be performed by the other party prior thereto have been satisfied and whether or not the other party is then in default in the performance of any covenant, agreement or condition contained in this Lease and specifying, if any, each such unsatisfied condition and each such default of which the signer may have knowledge; and

(iii) stating any other fact or certifying any other condition reasonably requested by Landlord or requested by any mortgagee or prospective mortgagee or purchaser of the Property or of any interest therein. It is intended that any statement delivered pursuant to the provisions of this Article be relied upon by any such purchaser or mortgagee.

(b) Intentionally Omitted.

31. **Severability**.

No determination or adjudication by any court, governmental or administrative body or agency or otherwise that any provision of this Lease or of any amendment hereto or modification hereof is invalid or unenforceable in any instance shall affect the validity or the enforceability

(a) of any other provision of this Lease, of such amendment or modification, or any other such amendment or modification, or

(b) of such provision in any other instance or circumstance which is not within the jurisdiction of such court, body or agency or controlled by its said determination or adjudication. Each and every provision hereof and of each such amendment or modification shall be and remain valid and enforceable to the fullest extent allowed by law, and shall be construed wherever possible as being consistent with applicable law.

32. **Miscellaneous**.

(a) The Building may be designated and known by any name Landlord may choose and such name may be changed from time to time at Landlord's sole discretion; provided, however, that Landlord shall not rename the Building at any time in which Tenant leases more than fifty percent (50%) of the rentable square footage thereof. The Titles appearing in connection with various sections of this Lease are for convenience only. They are not intended to indicate all of the subject matter in the text and they are not to be used in interpreting this Lease nor for any other purpose in the event of any controversy.

(b) the term "person" shall be deemed to mean a natural person, a trustee, a corporation, a partnership and any other form of legal entity;

(c) all references in the singular or plural number shall be deemed to have been made, respectively, in the plural or singular number as well. Each and every document or other writing which is referred to herein as being attached hereto or is otherwise designated herein as an exhibit hereto is hereby made a part hereof.

(d) Tenant shall pay within thirty (30) days following receipt of written demand all of Landlord's costs, charges and expenses, including the reasonable fees and out-of-pocket expenses of counsel, agents and others retained by Landlord, actually incurred in enforcing Tenant's obligations hereunder or incurred by Landlord in any litigation, negotiation or transaction in which Tenant directly causes Landlord without Landlord's fault to become involved or concerned. Notwithstanding the foregoing, if any legal action, suit or proceeding is commenced between Landlord and Tenant regarding their respective rights and obligations under this Lease, the prevailing party shall be entitled to recover, in addition to damages or other relief, costs and expenses, attorneys' fees and court costs (including, without limitation, expert witness fees). As used herein, the term "prevailing party" shall mean the party which obtains the principal relief it has sought, whether by compromise settlement or judgment. If the party which commenced or instituted the action, suit or proceeding shall dismiss or discontinue it without the concurrence of the other party, such other party shall be deemed the prevailing party.

(e) Intentionally deleted.

(f) No waiver of any provision of this Lease shall be implied by any failure of Landlord to enforce any remedy allowed for the violation of such provision, even if such violation is continued or repeated, and no express waiver shall affect any provision other than the one(s) specified in such waiver and only then for the time and in the manner specifically stated. No receipt of monies by Landlord from Tenant after the termination of this Lease shall in any way alter the length of the Term or of Tenant's right of possession hereunder or after the giving of any notice shall reinstate, continue or extend the Term or affect any notice given to Tenant prior to the receipt of such moneys, it being agreed that after the service of notice or the commencement of a suit or after final judgment for possession of the Premises subject to the terms of this Lease, Landlord may receive and collect any rent due, and the payment of said rent shall not waive or affect said notice, suit or judgment.

(g) It is mutually agreed by and between Landlord and Tenant that they hereby waive trial by jury in any action, proceeding or counterclaim brought by either of the

parties hereto against the other on any matter whatsoever arising out of or in any way connected with this Lease, the relationship of Landlord and Tenant, Tenant's use or occupancy of the Premises or claim of injury or damage.

(h) Tenant acknowledges and agrees that Landlord and Landlord's agents have made no representation, agreements, conditions, warranties, understandings, or promises, either oral or written, other than as herein set forth, with respect to this Lease, the Building, the Property, the Premises, or otherwise.

(i) Upon the expiration or other termination of this Lease, neither party shall have any further obligation nor liability to the other except as otherwise expressly provided in this Lease and except for such obligations as, by their nature or under the circumstances, can only be, or by the provisions of this Lease, may be performed after such expiration or other termination. Any claims by Landlord, including, but not limited to, Tenant's obligations, if any, to maintain or repair the Premises or to make improvements or alterations or to remove or restore such items must be represented in writing by Landlord to Tenant within nine (9) months (which time is of the essence) after expiration or termination of this Lease or shall be deemed irrevocably waived.

33. **Brokers**.

Landlord and Tenant each represent and warrant to the other that it did not deal with any broker, finder or other intermediary to whom a fee or commission is or will become payable in connection with this Lease except CBRE, Inc. (as representative for Landlord) and Gola Corporate Real Estate (as representative for Tenant) whose commission shall be paid by Landlord pursuant to separate agreement. Each party agrees to indemnify, defend and hold the other harmless from and against any loss, claim, expense or liability with respect to any commissions or brokerage fees claimed by any broker or finder other than the Broker on account of this Lease due to any action of the indemnifying party.

34. **Security Deposit**.

(a) Tenant, concurrently with the execution of this Lease, shall deliver to Landlord a letter of credit in the amount of $1,080,714.00 and meeting the criteria of **Exhibit "G"** (the "Letter of Credit") as security for the payment by Tenant of the Rent herein agreed to be paid and for the faithful performance of the covenants contained in this Lease. If at any time an Event of Default by Tenant shall occur and be continuing under any of the provisions of this Lease, Landlord shall be entitled, at its sole discretion to draw upon the Letter of Credit:

(i) to cover payment of

(A) any rent for the payment of which Tenant shall be in default as aforesaid

(B) any expense reasonably incurred by Landlord in accordance with this Lease in curing any such Event of Default, and/or

(C) any other sums due to Landlord in connection with such Event of Default or the curing thereof as provided for in this Lease, including, without limitation,

any damages incurred by Landlord by reason of such Event of Default as set forth in Article 21 above; or

(ii) to retain the same in liquidation of all or part of the damages suffered by Landlord by reason of such Event of Default. Any portion of such Letter of Credit which shall not be utilized for any such purpose shall be released to Tenant within forty five (45) days after the expiration of this Lease and surrender of the entire Premises to Landlord. In the event that Landlord shall apply some or all of the security deposit toward one or more of the items referred to in this Article 34 Tenant shall replenish the Letter of Credit in an amount equal to the sum so applied. Such replenishment shall be made by Tenant within ten (10) business days after Landlord's request therefor.

(b) Provided that no Event of Default beyond any applicable cure period by Tenant under this Lease has occurred and is continuing, the amount of the Letter of Credit will be reduced pursuant to the following schedule:

Date of Reduction	**Amount of Letter of Credit After Reduction**
First Day of the Thirty-Seventh (37th) Full Month of the Term	$750,000.00
First Day of the Sixty-First (61st) Full Month of the Term	$450,000.00
First Day of the Eighty-Fifth (85th) Full Month of the Term	$280,000.00

(c) The Letter of Credit may be issued by Pacific Western Bank or other issuer approved by Landlord in its reasonable discretion. If there occurs a material adverse change in the financial condition of Pacific Western Bank as reasonably determined by Landlord, Landlord may require that Tenant provide a cash Security Deposit in the then amount of the Letter of Credit.

(d) Transfer fees shall be payable by Tenant and not Landlord.

35. **Quiet Enjoyment**.

Tenant, upon paying the Fixed Rent, additional rent and all other charges herein provided for and observing and keeping all covenants, agreements and conditions of this Lease on its part to be kept, shall quietly have and enjoy the Premises during the term of this Lease without hindrance or molestation by anyone claiming by or through Landlord, subject, however, to the exceptions, reservations and conditions of this Lease.

36. **Rights of Mortgage Holder**.

If the holder of a mortgage covering the Premises shall have given prior written notice to Tenant that it is the holder of such mortgage and such notice includes the address at which notices to such mortgagee are to be sent and a request that Tenant include said mortgage holder as a notice recipient under this Lease, then Tenant agrees to give to such holder notice simultaneously with any notice given to Landlord to correct any default of Landlord as

hereinabove provided and agrees that the holder of record of such mortgage shall have the right, within the greater of thirty (30) days thereafter or the same period of time accorded Landlord under this Lease after receipt of said notice, to correct or remedy such default before Tenant may take any action under this Lease by reason of such default.

37. **Whole Agreement**.

It is expressly understood and agreed by and between all the parties hereto that this Lease and any riders attached hereto and forming part hereof set forth all the promises, agreements, warranties, representations and understandings between Landlord and Tenant relative to the Premises and this leasehold, and that there are no promises, agreements, conditions, warranties, representations or understandings, either oral or written, between them other than as herein set forth. It is further understood and agreed that, except as herein otherwise provided, no subsequent alteration, amendment, understanding or addition to this Lease shall be binding upon Landlord or Tenant unless reduced to writing and signed by them.

38. **Financial Statements**.

Upon the request of Landlord Tenant shall supply to Landlord copies of all of Tenant's and/or Guarantor's most recent quarterly or annual financial statements then available; provided however, Landlord shall not request such financial statements more frequently than two (2) times per calendar year so long as no Event of Default exists. To the extent such financial statement are not publicly available and accessible by Landlord, Tenant shall provide such financial statements to Landlord within fifteen (15) days after Landlord's request therefor and shall be kept confidential but may be disclosed to: (i) the extent required by law; and (ii) Landlord's employees and advisors (e.g. accountants, attorneys etc.) who are similarly bound by such confidentiality, to the extent necessary for Landlord to exercise its rights and fulfill its obligations under this Lease.

39. **Option to Extend Term**.

Provided that (i) Landlord has not given Tenant notice of a material non-monetary Event of Default or any monetary Event of Default more than two (2) times in the preceding 12-month period, (ii) there then exists no Event of Default by Tenant under the Lease nor any event that with the giving of notice and/or the passage of time would constitute an Event of Default, (iii) Tenant has not previously assigned this Lease or sublet all of the Premises (except as a Permitted Transfer), and (iv) Tenant's creditworthiness is equal to or greater than it was as of the date of this Lease (as reasonably determined by Landlord), Tenant shall have the right and option (an "Extension Option") to extend the Term for one (1) additional period of five (5) years, exercisable in the following manner. If Tenant is desirous of exercising the Extension Option under this section, Tenant shall give Landlord written notice not less than twelve (12) months in advance of the scheduled Expiration Date of Tenant's intention to extend the Term ("Tenant's Extension Notice"), it being agreed that time is of the essence and that the Extension Option is personal to Tenant and is non-transferable to any transferee or other party other than a Permitted Transferee. Promptly after receipt of Tenant's Extension Notice, Landlord and Tenant shall negotiate the Fixed Rent for the Extension Option in good faith. The Extension Option shall be under the same terms and conditions as provided in this Lease except as follows:

(a) the Extension Option period shall begin at the original Expiration Date and thereafter the Expiration Date shall be one hundred ninety (190) months from the Commencement Date;

(b) all references to the Term in this Lease shall be deemed to mean the Term as extended pursuant to this section;

(c) after the Extension Option provided herein, there shall be no further options to extend; and

(d) the Fixed Rent payable by Tenant shall be the then market rate as reasonably determined by Landlord and Tenant negotiating in good faith immediately following Landlord's receipt of the Tenant's Extension Notice.

40. **Expansion Option**.

(a) Those certain premises being suites 110 (approximately 8,231 rsf) and 112 (approximately 4,824 rsf), in the Building located on the first floor and as shown on **Exhibit "H"** attached hereto (each an "Expansion Space") are, as of the date of this Lease, not leased to another party. If, on or before April 1, 2017 (the "Outside Offer Date"), Tenant desires to lease any or all of the Expansion Spaces, Tenant shall have the exclusive option (the "Expansion Option") to expand the size of the Premises to include any or all of the Expansion Space(s) (the "Expansion Option") by providing written notice to Landlord of such intention (the "Tenant Expansion Notice"). Provided Landlord receives the Tenant Expansion Notice prior to the Outside Offer Date, Tenant's lease of the subject Expansion Space shall be pursuant to the terms of this Lease except that: (i) the financial terms for Tenant's lease of the subject Expansion Space shall be consistent with the terms of this Lease with respect to Fixed Rent/rsf and scheduled escalations for the Premises as set forth in Section 4 of the Lease; (ii) the commencement date of the lease of the Expansion Space shall be the date that is 150 days following the exercise of the Expansion Option and the term shall be coterminous with the Term set forth in Section 3(a); (iii) the subject Expansion Space shall be leased in its "as is", "where is" condition and Landlord shall have no obligations whatsoever to improve or pay to improve the Expansion Space for Tenant's use or occupancy, provided that Landlord shall provide Tenant with an additional allowance to improve the subject Expansion Space with such allowance to be equal to $00.32308/rsf for each month of the Expansion Space term (for example, if the Expansion Space term commenced August 1, 2017, for Suite 110, the allowance would equal 129 months x $00.32308 x 8,231 = $343,046.02); (iv) Tenant's Proportionate Share shall be increased pro rata; (v) the Security Deposit will increase on a pro rata basis determined by Fixed Rent payable before and after the lease of the Expansion Space; and (vi) Fixed Rent, but not Tenant Energy Costs, shall be conditionally abated at the rate equal to $00.17147/rsf for each month of the Expansion Space term (for example, if the Expansion Space term commenced August 1, 2017, for Suite 110, the abatement would equal 129 months x $00.17147 x 8,231 = $182,066.67) to be applied 50% to the first 5 months and 50% during months 13-17 of the Expansion Space term. Any improvements made to the Expansion Space shall be made by Landlord subject to the terms of Section 8, with a management fee payable to $1.02/rsf for the Expansion Space improvements plus two percent (2%) of the net cost increase or decrease resulting from any Change Order.

(b) Notwithstanding anything to the contrary contained in this Lease, the term of the Lease for the Expansion Space shall expire on the date set forth in this Lease as the Expiration Date (as the same may be extended pursuant to Section 39 hereof).

(c) If (i) Tenant does not notify Landlord prior to the Outside Offer Date that Tenant desires to lease the Expansion Space, this Expansion Option shall terminate and the Expansion Space shall after such Outside Offer Date be deemed an Un-Leased RFO Space as defined in Section 41 of the Lease and shall thereafter be subject to the terms and conditions as set forth in Section 41.

(d) If Tenant exercises the Expansion Option, the space described in Tenant's Expansion Notice will be deemed a part of the Premises under this Lease whether or not a lease amendment is signed, but upon written request of Landlord, Tenant shall execute an amendment to this Lease incorporating such terms within ten (10) business days of Landlord's request.

(e) Time is of the essence with respect to Tenant's obligations hereunder.

41. **Right of First Offer**.

Spaces in the Building located on the first floor as shown on **Exhibit "I"** attached hereto (each an "RFO Space") are, as of the date of this Lease, either currently available for lease ("Un-leased RFO Space") or leased to other tenants (together with any assignees, each a "Current Tenant") ("Leased RFO Space"). If (i) Landlord has not given Tenant notice of a material non-monetary Event of Default or any monetary Event of Default more than two (2) times in the preceding 12-month period, (ii) there then exists no Event of Default by Tenant under the Lease nor any event that with the giving of notice and/or the passage of time would constitute an Event of Default, (iii) Tenant has not previously assigned this Lease or sublet all of the Premises (except as a Permitted Transfer), and (iv) Tenant remains creditworthy, as reasonably determined by Landlord, Tenant shall have the one-time right of first offer with respect to each RFO Space (each an "RFO Option") to extend this Lease to include the then available RFO Space for a term coterminous with the Term of this Lease, as it may be extended or renewed, but in no event less than three (3) years, in the following manner, it being agreed that time is of the essence and that each RFO Option is non-transferable to any sublessee or any party other than a permitted transferee of this Lease. Notwithstanding the foregoing, Suites 110 and 112 which are unleased as of the date of this Lease and are defined as Option Spaces in Section 40 will not be considered as Un-leased RFO Space unless and until April 1, 2017, if Tenant has not exercised the Option described in Section 40 with respect to either or both Option Spaces.

(a) With respect to Leased RFO Space:

(i) Landlord shall notify Tenant from time to time when the Leased RFO Space or any portion thereof becomes available for lease to third parties, advising Tenant in writing of Landlord's offer to lease to Tenant the then available Leased RFO Space and the terms to be applicable to the lease of the available Leased RFO Space, for a term of not less than three (3) years ("Landlord's Notice of RFO Terms"). Within ten (10) business days following Tenant's receipt of Landlord's Notice of RFO Terms, Tenant shall notify Landlord in writing of Tenant's intention to exercise its RFO Option with respect to the space described in Landlord's Notice of

RFO Terms ("Tenant's Response") and concurrently with such exercise, Tenant may, at its option, object to the proposed Fixed Rent contained in Landlord's Notice of RFO Terms, in which case the parties shall negotiate in good faith to agree upon such Fixed Rent amount; pending agreement of the parties the Fixed Rent shall be the proposed Fixed Rent contained in Landlord's Notice of RFO Terms. If Tenant exercises the RFO Option, the space described in Landlord's Notice of RFO Terms will be deemed a part of the Premises under this Lease whether or not a lease amendment is signed, but upon written request of Landlord, Tenant shall execute an amendment to this lease incorporating such terms within ten (10) business days of Landlord's request.

(ii) If Tenant does not issue the Tenant Response within such ten (10) business day period or issues the Tenant Response and elects not to lease the available Leased RFO Space, then Landlord shall have the right to lease all or part of space to any other party at any time on any terms and conditions acceptable to Landlord.

(b) With respect to Un-leased RFO Space:

(i) Tenant may at any time prior to the lease of the Un-leased RFO Space by Landlord to another party, advise Landlord of Tenant's interest in leasing the Un-leased RFO Space by providing written notice to Landlord. Landlord shall then advise Tenant of Landlord's Notice of RFO Terms. Within ten (10) business days following Tenant's receipt of Landlord's Notice of RFO Terms, Tenant shall send Tenant's Response with respect to the space described in Landlord's Notice of RFO Terms, in which, Tenant may, at its option, object to the proposed Fixed Rent contained in Landlord's Notice of RFO Terms, in which case the parties shall negotiate in good faith to agree upon such Fixed Rent amount; pending agreement of the parties the Fixed Rent shall be the proposed Fixed Rent contained in Landlord's Notice of RFO Terms. If Tenant exercises the RFO Option, the space described in Landlord's Notice of RFO Terms will be deemed a part of the Premises under this Lease whether or not a lease amendment is signed, but upon written request of Landlord, Tenant shall execute an amendment to this lease incorporating such terms within ten (10) business days of Landlord's request.

(ii) If Tenant does not issue the Tenant Response within such ten (10) business day period or issues the Tenant Response and elects not to lease the available Leased RFO Space, then Landlord shall have the right to lease all or part of space to any other party at any time on any terms and conditions acceptable to Landlord.

(iii) If Landlord shall lease any of Un-leased RFO Space to a third-party and such lease shall expire or terminate then such lease shall constitute a "Current Lease" and this Section shall again be applicable to such Available RFO Space.

(c) If Tenant exercises an RFO Option with respect to any Available RFO Space, then:

(i) Tenant's proportionate share will increase on account of the addition of such Available RFO Space;

(ii) Tenant's exercise of the RFO Option shall specify the area of the then Available RFO Space which Tenant elects to lease, which shall be subject to Landlord's reasonable determination that any remaining Available RFO Space not leased by Tenant is marketable to other tenants;

(iii) the commencement date of the lease of the Available RFO Space will be the later of the date of Tenant's exercise of the RFO Option, or the date on which such Available RFO Space is delivered to Tenant for the commencement of Tenant's improvements thereto, vacant and free and clear of any tenancies or claims of tenancies, including the expiration or sooner termination of the Current Lease or any subsequent lease thereof, but in no event later than the commencement of Tenant's business operations in such Available RFO Space; and

(iv) the expiration date of the lease of the Available RFO Space will be the date upon which the Term of this Lease is naturally set to expire; provided that if the Expiration Date of the Term of the Lease is less than three (3) years from the commencement date of the lease of the Available RFO Space, Tenant shall first be obligated to exercise its Extension Option as set forth in Section 39 above thereby extending the Term of the Lease for a period of five (5) years.

42. **Vent Installation**.

If Tenant (i) exercises the Expansion Option for Suite 110 before April 1, 2017, to be used as laboratory space, Tenant shall have the non-exclusive right to use, install, maintain and repair a roof vent ancillary to Tenant's permitted Use (the "Roof Installation") on the roof of the Building and related equipment and enclosures in a closet (no larger than 50 square feet) on the third floor of the Building (the "Vent Equipment"), through a chase in the Building at the location shown on **Exhibit "J"**; or (ii) if Tenant does not exercise an Expansion Option before April 1, 2017 for Suite 110 to be used as laboratory space, but at any time leases other space in the Building for use as laboratory space, Tenant will have the right to a Roof Installation and Vent Equipment at a location be mutually agreed by Landlord and Tenant to be negotiated in good faith, in either instance to be under and subject to the following conditions:

(a) Tenant shall comply with all laws and shall obtain, and deliver to Landlord written evidence of, any approval(s) required under any recorded covenants or restrictions applicable to the Property.

(b) Tenant shall obtain Landlord's prior approval of the size, location, clearance from fresh air intake for the Building, effect on Building systems, lack of visibility from the ground and the plans and specifications for the proposed Roof Installation and Vent Equipment in accordance with Section 9 of this Lease, which approval shall not be unreasonably withheld, conditioned or delayed. Contemporaneously with Landlord's review per Section 9 of this Lease, Landlord shall submit the plans and specifications to its roofing contractor for comment. Tenant shall pay all reasonable, actual out-of-pocket costs incurred by Landlord for architectural, engineering, and roofing contractors review.

(c) Tenant shall comply with all provisions of this Lease pertaining to such installation, specifically including Section 9 of this Lease.

(d) At least three (3) business days prior to installation, Tenant shall notify Landlord of the date and time of the installation, and Landlord may have a representative present during the installation.

(e) Tenant shall maintain the Roof Installation and Vent Equipment in a safe, good and orderly condition. The installation, maintenance, repair and removal of the Roof

Installation and Vent Equipment shall be performed at Tenant's sole expense in a manner which will not impair the integrity of, damage or adversely affect the warranty applicable to, the roof or any other portion of the Building.

(f) No later than the expiration or sooner termination of the Term, at Tenant's sole expense, Tenant shall remove the Roof Installation if required by Landlord.

(g) Tenant's indemnification of Landlord pursuant to this lease also applies to the Roof Installation and the Vent Equipment and Tenant's use of any portion of the Building therefor.

(h) The Roof Installation and the Vent Equipment use shall be solely for Tenant's use (or other tenants of the Building so long as Tenant's use is not adversely impacted, as determined by Landlord and Tenant negotiating in good faith) and not for the benefit or use of any third party (e.g., for rental purposes).

43. **Generator and Air Handling Unit**.

If Tenant (i) exercises the Expansion Option for Suite 110 before April 1, 2017, to be used as laboratory space, or (ii) if Tenant does not exercise an Expansion Option before April 1, 2017 for Suite 110 to be used as laboratory space, but at any time leases other space in the Building for use as laboratory space, Tenant, at Tenant's sole cost and expense, shall have the right and option to install a generator (the "Generator") to furnish electrical power for Tenant's operation in the Premises in the case of loss of commercial power and an air handling unit (the "AHU") to supply air to the laboratories in Suite 110, in the respective locations shown in **Exhibit "K".** The AHU will have a duct measuring approximately 6' x 3' that will enter the Building in the location shown on **Exhibit "K"**. Tenant, using the Tenant Allowance or at Tenant's sole cost and expense, shall (i) install screening, landscaping or other improvements reasonably satisfactory to Landlord in order to satisfy Landlord's aesthetic requirements in connection with the Generator and AHU, (ii) obtain Landlord's prior approval (not to be unreasonably withheld, conditioned or delayed) of the make and model of the Generator and AHU that Tenant proposes to install, not to be unreasonably withheld; (iii) operate, maintain and repair the Generator and AHU in good condition and in accordance with applicable laws throughout the Term of the Lease; and (iv) minimize the noise disturbance to other tenants of the Building. Landlord shall have the right, upon the expiration or any termination of the Lease, to require Tenant to remove the Generator and AHU at Tenant's sole cost and expense and to restore the Property to the condition which existed prior to the installation of the Generator and AHU. Tenant shall be responsible for all costs to repair damage caused to any portion of the Property caused by such removal and all restoration costs. Notwithstanding the foregoing, at Tenant' s sole cost, Tenant will enter into a standard maintenance contract for the generator and AHU on terms meeting reasonable specifications provided to Tenant by Landlord from time to time, and subject to Landlord's approval, such approval not to be unreasonably withheld, conditioned or delayed. Tenant shall provide copies of its then in effect maintenance contracts to Landlord.

44. **Tenant's Property.**

Landlord shall not have, and hereby waives, any security interest or lien (express, implied, statutory or otherwise) on Tenant's furniture, equipment, trade fixtures and personal property (collectively, "Tenant's Property"). Upon Tenant's written request, Landlord shall execute a waiver in the form attached hereto as **Exhibit "L"** (or such other commercially reasonable waiver form), of any right, title, lien, or interest in Tenant's Property.

[signatures on following page]

IN WITNESS WHEREOF, the parties hereto have executed this Lease the day and year set forth above.

LANDLORD:

CHESTERBROOK PARTNERS, LP,
a Delaware limited partnership

By: Tredyffrin GP, LLC,
a Delaware limited liability company,
its general partner

By: /s/ Mark Pasierb
Mark Pasierb
President

TENANT:

TREVENA, **INC**., a Delaware corporation

By: /s/ John M. Limongelli

Name: John M. Limongelli

Its: SVP, General Counsel & Chief Administrative Officer

WAIVER OF PRIOR HEARING CERTIFICATION

The undersigned acknowledges that the above Lease authorizes and empowers Landlord upon an Event of Default, without prior notice or a prior hearing, to cause the entry of judgments against the undersigned for possession of the Premises and immediately thereafter, without prior notice or a prior hearing, to exercise post-judgment enforcement and execution remedies.

The undersigned acknowledges that the undersigned has agreed to waive the undersigned's rights to prior notice and a hearing under the Constitution of the United States, the Constitution of the Commonwealth of Pennsylvania and all other applicable state and federal laws, in connection with Landlord's ability to cause the entry of judgments against the undersigned and immediately thereafter exercise Landlord's post-judgment enforcement and execution remedies (which may include removal of the undersigned from the Premises by law enforcement officers). The undersigned's counsel has reviewed the legal impact of this waiver with the undersigned, and the undersigned acknowledges that the undersigned has freely waived such rights.

Trevena, Inc., a Delaware corporation

By: _____

Name: _____

Title: _____

Dated: December ___, 2016

COMMONWEALTH OF PENNSYLVANIA :
: ss:
COUNTY OF _____ :

On this _____ day of _____, 2016, before me, a Notary Public, personally appeared _____, who acknowledged himself/herself to be the _____ of _____, a _____ _____, and that he/she in such capacity, being authorized to do so, executed the foregoing Lease Agreement for the purposes therein contained.

IN WITNESS WHEREOF, I have hereunder set my hand and official seal.

_____
NOTARY PUBLIC
My commission expires:

EXHIBIT "A"

FLOOR PLAN

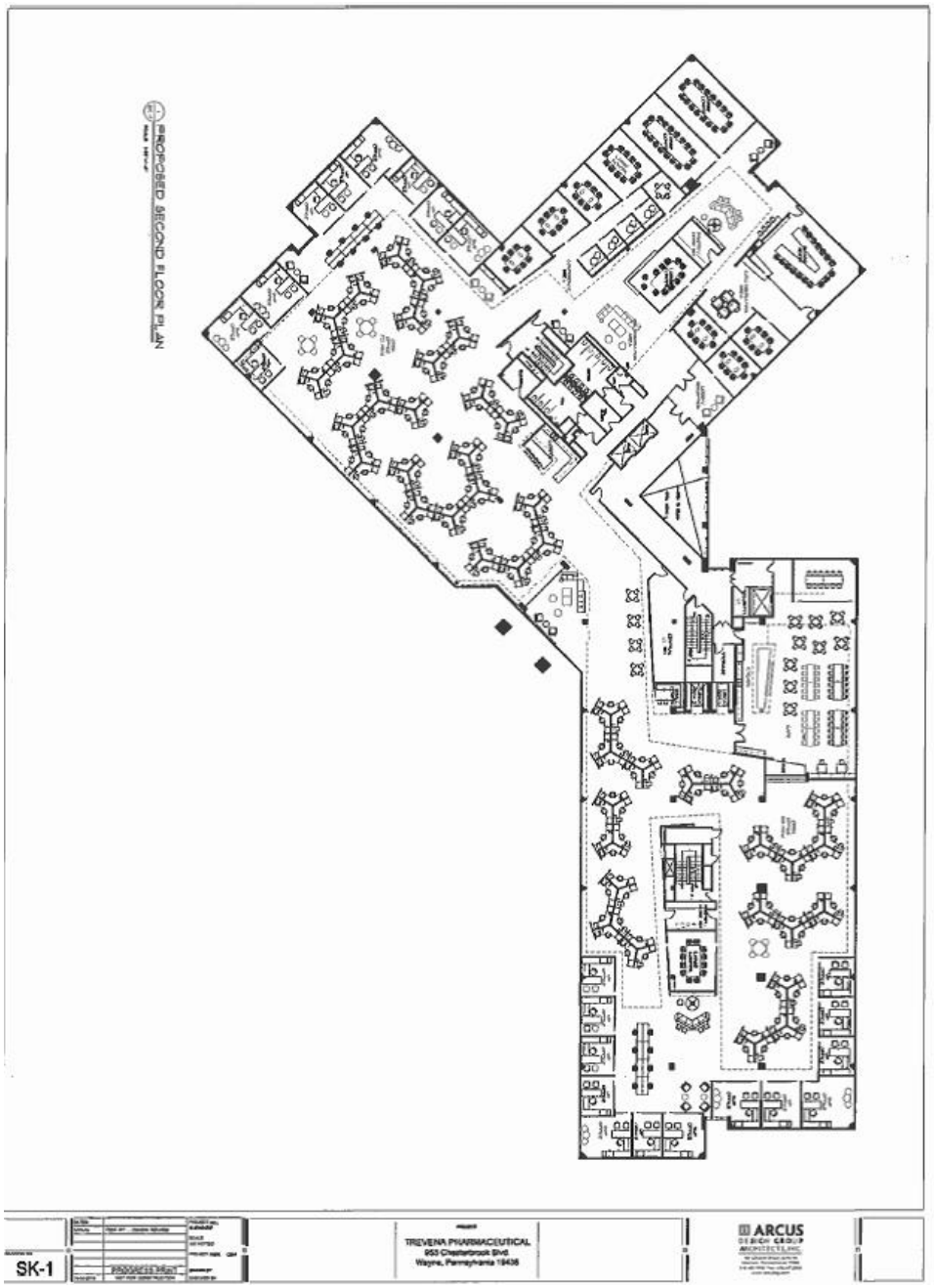


EXHIBIT "B"

DESCRIPTION OF THE LAND

955 CHESTERBROOK BOULEVARD - METES AND BOUNDS

Tredyffrin Township, Chester County, PA

ALL THAT CERTAIN Unit designated as Unit Number I (formerly Unit Number 3), being a Unit in Parcel 9 Condominium, situate in the Township of Tredyffrin, County of Chester and Commonwealth of Pennsylvania, as designated in the Declaration of Condominium of Parcel 9 Condominium, bearing date the 27th day of December A. D., 1985 and recorded in the Office for the Recording of Deeds in and for the County of Chester, Commonwealth of Pennsylvania on the 30th day of December A.D., 1985 in Record Book 174 page 108, etc., as amended by First Amendment to Declaration of Condominium bearing date the 28th day of April A.D., 1986 and recorded the 27th day of May A.D., 1986 in Record Book 298 page 534, and as further amended by Second Amendment to Declaration of Condominium bearing date the 6th day of April A.D., 1987 and recorded in Record Book 698 page 164 and as further amended by Third Amendment to Declaration of Condominium bearing date the 18th day of December, 1987 and intended to be recorded and a Declaration Plat for Parcel 9 Condominium bearing date the 9th day of December A.D., 1985 and recorded as Exhibit "C" to the Declaration of Condominium of Parcel 9 Condominium in Record Book 174 page 108 and as last revised the 2nd day of April A.D., 1987 and recorded as Exhibit "C" with the Second Amendment to the Declaration in Record Book 698 page 164.

TOGETHER with all right, title and interest, being a 50.00% undivided interest of, in and to the common elements as set forth in the aforesaid Declaration of Condominium and amendments thereto.

PARCEL #43-5-26.3C.

BEING known as 955 Chesterbrook Boulevard.

BEING the same premises which One Twenty Associates, L.P., a Delaware Limited Partnership by Deed dated 1/4/1988 and recorded 1/6/1988 in the County of Chester in Record Book 1020 page 67, conveyed unto DWR Chesterbrook Associates, a Pennsylvania General Partnership, in fee.

EXHIBIT "C"

MEMORANDUM OF COMMENCEMENT DATE

THIS MEMORANDUM OF COMMENCEMENT DATE made this ____ day of _____, 20___.

CHESTERBROOK PARTNERS, LP ("Landlord") and **TREVENA, INC.** ("Tenant") are parties to a certain Agreement of Lease ("Lease") dated _____, 20___ with respect to premises identified as Suites _____ at _____.

_____ Pursuant of the Lease, Landlord and Tenant do hereby confirm that the Term of the Lease commenced _____, 20___ and, subject to such rights of renewal or extension, if any, as are expressly provided therein, shall expire _____.

IN WITNESS WHEREOF, Landlord and Tenant have executed this Memorandum the day and year first above written.

LANDLORD:
CHESTERBROOK PARTNERS, LP,
a Delaware limited partnership

By: Tredyffrin GP, LLC,
a Delaware limited liability company,
its general partner

By: _____

TENANT:
TREVENA, INC., a Delaware corporation

By: _____

Name: _____

Its: _____

EXHIBIT "D"

EARLY ACCESS BY TENANT

Landlord shall permit Tenant and its agents to enter the Premises fourteen (14) days prior to the Commencement Date as reasonably estimated by Landlord in order that Tenant may perform through its own contractors such other work and decorations as Tenant may desire at the same time that Landlord's contractors are working in the space. The foregoing approval to enter prior to the Commencement Date, however, is conditioned upon Tenant's workmen and mechanics working in harmony and not unreasonably interfering with the labor employed by Landlord, Landlord's mechanics or contractors or by any other tenant or their contractors and compliance with the terms of the Lease except as to the covenant to pay rent. If at any time, such entry shall cause material disharmony or interference therewith, this license may be withdrawn by Landlord upon twenty-four (24) hours written notice to Tenant and further provided that Workmen's Compensation as required by law and Public Liability Insurance and Property Damage Insurance, all in amounts and with companies and on forms reasonably satisfactory to Landlord, shall be provided to Landlord and at all times maintained by Tenant's contractors engaged in the performance of the work, and before proceeding with work, certificates of such insurance shall be furnished to Landlord.

Such entry shall be deemed to be under all of the terms, covenants, provisions and conditions of the said Lease except as to the covenant to pay rent. Landlord shall not be liable in any way for any injury, loss or damage which may occur to any of Tenant's decorations or installations so made prior to the commencement of the term of the Lease, the same being solely at Tenant's risk.

The provisions of this Exhibit "D" are specifically subject to the provisions of the Lease.

EXHIBIT "E"

RULES AND REGULATIONS

1. The walkways, roadways, driveways, entrances, lobbies, passages, and stairways shall not be obstructed by Tenant or used by Tenant for any purposes other than ingress and egress from and to the Building and Tenant's offices. The parking areas shall be used only for the parking of automobiles of Tenant, its agents, employees and invitees while actually present in the Premises. Landlord shall in all cases retain the right to control or prevent access to all of the aforesaid areas of all persons whose presence, in the reasonable judgment of Landlord, shall be prejudicial to the safety, peace, character, or reputation of the Building, the property located therein or of any of the tenants.

2. The toilet rooms, water closets, sinks, faucets, plumbing or other service apparatus of any kind shall not be used by Tenant for any purposes other than those of which they were installed, and no sweepings, rubbish, rags, ashes, chemicals or other refuse or injurious substances shall be placed therein or used in connection therewith by Tenant or left by Tenant in the lobbies, passages, elevators or stairways. Nothing shall be thrown by Tenant or Tenant's employees nor be allowed by them to drop out of the windows or doors, or down the passages of the Building. Any water lines installed by Tenant for purposes of running coffee makers, refrigerators, ice makers, etc., within the Premises, must be copper (not PVC).

3. Nothing shall be placed by Tenant on the outside of the Building or on its window sills or projections. Skylights, windows, doors and transoms shall not be covered or obstructed by Tenant, and no window shades, blinds, curtains, screens, storm windows, awnings or other materials shall be installed or placed on any of the windows or in any of the window spaces, except as approved in writing by Landlord (which approval shall not be unreasonably withheld, conditioned or delayed).

4. Except as set forth in Section 16 in the Lease, no sign, lettering, insignia, advertisement, notice shall be inscribed, painted, installed or placed on any windows or in any window spaces or any other part of the outside or inside of the Building, unless first approved in writing by Landlord (which approval shall not be unreasonably withheld, conditioned or delayed). Names on or beside suite entrance doors shall be provided for Tenant by Landlord and not otherwise, and at Landlord's expense; in all instances, such names shall be of design and form first approved by Landlord.

5. Except as permitted pursuant to Rules numbered 9 and 13, Tenant shall not place additional locks upon any doors. The janitor and the manager of the Building may at all times keep a pass key, and he and other agents of the Landlord shall at all times be allowed admittance to the leased Premises in accordance with and for purposes permitted in Tenant's lease. Upon surrendering possession of the Premises at the termination of this Lease, Tenant shall deliver to Landlord all keys for the Premises.

6. No bicycles or similar vehicles will be allowed in the Building.

7. Tenant shall not do or commit, or suffer to be done or committed, any act or thing whereby, or in consequence whereof, the rights of other tenants will be unreasonably obstructed

or interfered with, or other tenants will in any other way be unreasonably injured or annoyed, or whereby the Building will be damaged. Tenant shall not suffer or permit the Premises or any part thereof to be used in any manner or anything to be done therein or suffer or permit anything to be brought into or kept in the Premises which, in the reasonable judgment of Landlord, shall in any way impair or tend to impair the character, reputation or appearance of the Building as a first-class office building. Except as permitted pursuant to Section 15 of the Lease, Tenant shall neither bring, keep or use in the Building any chemical reagent except as the same may be components of commercial products normally used or consumed by occupants of office buildings. No birds, fish or other animals shall be brought into or kept in or about the Premises.

8. Tenant shall be solely responsible, at Tenant's sole cost and expense, for all maintenance and repairs to appliances (including but not limited to refrigerators, dishwashers, kitchen hot water heaters, etc.) whether installed by Landlord or Tenant or a prior tenant or any other party; provided, however, if Landlord has installed the appliance, Tenant will have the benefit of any applicable warranty.

9. In order that the Premises may be kept in a good state of preservation and cleanliness, Tenant shall during the continuance of its possession permit Landlord's employees and contractors and no one else to clean the Premises. Landlord shall be in no way responsible to Tenant for any damage done to furniture or other effects of Tenant or others by any of Landlord's employees, or any other person, or for any loss of Tenant's employees, or for any loss of property of any kind in or from the Premises, however occurring, except to the extent caused by the gross negligence or willful misconduct of Landlord, its agents, employees, or contractors. Tenant shall see each day that the windows are closed, lights are turned off, and the doors securely locked before leaving the Premises.

10. If Tenant desires to introduce signaling, telegraphic, telephonic, protective alarm or other wires, cables, apparatus or devices, Landlord shall direct where and how the same are to be placed, and except as so directed, no installation, boring or cutting shall be permitted. Landlord shall have the right to prevent and to cut off the transmission of excessive or dangerous current of electricity or annoyances into or through the Building or Premises and to require the changing of wiring connections or layout at Tenant's expense, to the extent that Landlord may deem reasonably necessary, and further to require compliance with such reasonable rules as Landlord may establish relating thereto, and in the event of non-compliance with the requirements or rules, Landlord shall have the right immediately to cut wiring or to do what it considers necessary to remove the danger, annoyance or electrical interference with apparatus in any part of the Building. All wires and cables installed by Tenant must be clearly tagged at the distributing boards and junction boxes and elsewhere required by Landlord, with the number of the office to which said wires and cables lead, and the purpose for which the wires and cables respectively are used, together with the name of the concern, if any, operating same.

11. A directory on a bulletin board on the ground floor may be provided by Landlord, on which the name of Tenant may be placed.

12. No furniture, packages, equipment, supplies or merchandise of Tenant will be received in the Building, or carried up or down in the elevators or stairways, except during such hours as shall be reasonably designated by Landlord, and Landlord in all cases shall also have the exclusive right to prescribe the method and manner in which the same shall be brought in or

taken out of the Building. Landlord shall in all cases have the right to exclude from the Building heavy furniture, safes and other articles which may be hazardous or to require them to be located at designated places in the Premises. The cost of repairing any damage to the Building caused by taking in or out furniture, safes or any articles or any damage caused while the same shall be in the Premises, shall be paid by Tenant.

13. Without Landlord's written consent, not to be unreasonably withheld, nothing shall be fastened to, nor shall holes be drilled or nails or screws driven into walls or partitions; nor shall walls or partitions be painted, papered or otherwise covered or moved in any way or marked or broken; nor shall any connection be made to electric wires for running fans or motors or other apparatus, devices or equipment; nor shall machinery of any kind other than customary small business machines be allowed in the Premises; nor shall Tenant use any other method of heating, ventilating, air conditioning or air cooling than that provided by Landlord. Telephones, switchboards and telephone wiring and equipment shall be placed only where designated by Landlord. No mechanics shall be allowed to work in or about the Building other than those employed by Landlord without the written consent of Landlord first having been obtained, such consent not to be unreasonably withheld. Notwithstanding the foregoing, Tenant is expressly permitted to, without prior consent from Landlord, hang pictures on the walls of the Premises.

14. Tenant shall be solely responsible, at Tenant's sole cost and expense, for providing security for the Premises at such times and in such fashion as Tenant shall deem reasonable or necessary, including but not limited to electronic or video surveillance or security. Landlord shall not be responsible or otherwise liable for, and Tenant expressly indemnifies Landlord from, any claim, loss or damage resulting from or arising out of any party's unauthorized access to the Premises, whether during or outside of normal business hours. Any re-keying or other repairs or improvements to the Premises required as a result of Tenant's security measures set forth herein shall be performed by Landlord (or Landlord's contractor) at Tenant's sole cost and expense.

15. Landlord shall, in no case, be liable or responsible for the admission or exclusion of any person to or from the Building or access to the Premises. In case of invasion, hostile attack, insurrection, mob violence, riot, public excitement or other commotion, explosion, fire or any casualty, Landlord reserves the right to bar or limit access to the Building for the safety of occupants or protection of property.

16. Upon reasonable prior written notice to Tenant, Landlord reserves the right to rescind, suspend or modify any rules or regulations and to make such other rules or regulations as, in Landlord's reasonable judgment, may from time to time be needful for the safety, care, maintenance, operation and cleanliness of the Building as a first class office building, or for the preservation of good order therein. Notice of any action by Landlord referred to in this paragraph, given to Tenant, shall have the same force and effect as if originally made a part of the foregoing Lease. New rules or regulations will be generally applicable to all tenants of the Building and will not, however, be unreasonably inconsistent with the proper use and enjoyment of the Premises by Tenant under the Lease and shall not materially increase Tenant's obligations or reduce its rights under this Lease.

17. The use of rooms as sleeping quarters is prohibited at all times.

18. Tenant shall keep the windows and doors of the Premises, including those openings on corridors and all doors between rooms or spaces entitled to receive heating, ventilating or air conditioning service and rooms and spaces not entitled to receive such service, closed during the respective times that the heating, ventilating or air conditioning system is operating, in order to conserve the service and effectiveness of the heating, ventilating or air conditioning system as the case may be. Tenant shall comply with all reasonable rules and regulations from time to time promulgated by Landlord to conserve such services.

19. Landlord reserves the right to require that the Premises or any portion thereof shall not be used by Tenant or others for an employment agency, or for securing employees other than those to be employed on the Premises, or for the payment of salaries or wages to employees or persons who are not actually employed in the Building, nor for any other purpose except that specified in this Lease.

20. Landlord shall have the right to enter the Premises to put a "To Let" or similar notice upon the Premises, which notice shall not be removed or obliterated by the Tenant, during the six months previous to the expiration of the then current Term of this Lease, and any such entering shall not be treated as a deprivation of Tenant's use of the Premises or work an eviction of Tenant or a recession of this Lease.

21. No smoking of any kind shall be permitted on the Property or in the Premises except within enclosed automobiles or similar vehicles or in other areas specifically designated by Landlord, if any.

22. Tenant shall be permitted to install a "Wi-Fi" or other communication system within the Premises for Tenant's sole use so long as such communication system does not interfere with or detract from another tenant's quiet enjoyment of its premises or otherwise interfere with Landlord's use, operation or maintenance of the Building or Property.

23. These rules and regulations are not intended to give Tenant any rights or claims in the event the Landlord does not enforce any of them against any other tenants or if Landlord does not have the right to enforce them against any other tenants and such non-enforcement will not constitute a waiver as to Tenant.

24. All paintings, application of wall covering(s) and other improvements made by Tenant within the Premises to the extent permitted under this Lease shall be made during non- business hours unless Landlord shall otherwise authorize in writing.

EXHIBIT "F"

CLEANING SPECIFICATIONS

General cleaning: five nights per week, Monday through Friday, excluding any laboratory space of Tenant (except where noted by "**" below).

DAILY:

1. Empty waste receptacles and remove to designated area for pick-up.**

2. Empty, wipe clean all ash trays. Where sand urns are used, empty all debris, smooth sand and replace when needed.

3. Dust and/or damp wipe clean the following:

   Desk
   Doors
   Chairs
   Pushplates
   Window sills
   Tables and Lamps
   Picture and Frames
   File and Storage Cabinets
   Counter, ledges, shelves & ventilation louvers under six feet

4. Spot vacuum all areas as needed.

5. Special attention will be given to the Executive areas, Conference rooms, and kitchen and break areas. Wipe clean all countertops, tables, refrigerators and microwaves, and wet mop kitchen and break room floors.

6. Wash, clean and disinfect all water fountains and/or coolers.

7. Wash front door glass, as well as the adjacent architectural metal trim, to remove fingerprints, smudges, etc. caused during the day.

8. Special attention will be given to the lobby, reception and other public areas. All furniture will be hand wiped and carpets thoroughly vacuumed.

9. Sweep all resilient tile floor coverings with chemically-treated dry mop. Spot mop to remove soilage.**

10. Extinguish all interior lights unless otherwise notified. Night and safety lights will be operated as instructed. All doors will be locked and secured and any doors that are not functioning will be reported by the night supervisor.**

11. Lavatories:

a. Sweep and wet mop floors

b. Polish all mirrors, bright work and enameled surfaces

c. Wash and disinfect all basins, bowls and urinals

d. Hand dust and clean all partitions, tops of tile ledges, all towel, paper and sanitary napkin dispensers.

e. Refill all toilet tissue, soap, sanitary napkin and towel dispensers (towels, tissues, napkins, hand soap, etc. to be supplied by Landlord).

WEEKLY:

1. Spot clean doors, glass partitions and electric switch plates. Glass doors will be washed.**
2. High dust all horizontal surfaces above the reach of the average person (such as door frames, partitions, ledges, etc.)**
3. All carpeted areas will be thoroughly vacuumed.
4. Remove fingerprints and scuff marks from all vertical surfaces within the reach of the average person.
5. Sweep or vacuum stairs, spot mop when required; dust handrails and riser. Polish trim where required.
6. Wet mop all non-carpeted floors and mats.**

MONTHLY:

1. Spray buff all resilient tile floors.**

QUARTERLY:

1. Dust venetian blinds.**

SEMI-ANNUALLY:

1. Wash windows inside and outside.**

EXHIBIT "G"

Letter of Credit Requirements

a. Letter of Credit as Security Deposit. Tenant shall deliver to Landlord (as beneficiary), and a copy to Landlord's attorney, a standby letter of credit in the amount of $1,080,700.00 (subject to reduction as set forth in Section 34 of the Lease) in form and content satisfying the requirements of this **Exhibit "G"**.

b. Requirements of Letter of Credit. The Letter of Credit shall be, among other things:

(i) subject to the International Standby Practices 1998, International Chamber of Commerce Publication No. 590;

(ii) irrevocable and unconditional;

(iii) in the amount of $1,080,700.00 (subject to reduction as set forth in Section 34 of the Lease);

(iv) conditioned for payment solely upon presentation of the Letter of Credit and a sight draft (or Landlord, at its election, may require a uniform form of non-presentment letter of credit); facsimile presentation is permitted; and

(v) transferable one or more times by Landlord without the consent of Tenant at Tenant's cost.

c. Issuing Bank. Subject to Section 34 of the Lease, the Letter of Credit shall be issued by a member of the New York Clearing House Association or a commercial bank or trust company reasonably satisfactory to Landlord.

d. Expiration or Reduction of Letter of Credit. The Letter of Credit shall expire not earlier than 12 months after the date of delivery thereof to Landlord and shall provide that same shall be automatically renewed for successive 12-month periods through a date which is not earlier than 90 days after the expiration date of this Lease, or any renewal or extension thereof, unless written notice of nonrenewal has been given by the issuing bank to Landlord and Landlord's attorney by registered or certified mail, return receipt requested, not less than 90 days prior to the expiration of the current period. If the issuing bank does not renew the Letter of Credit, and if Tenant does not deliver a substitute Letter of Credit at least thirty (30) days prior to the expiration of the current period, then, in addition to its rights granted under Section 27 of the Lease, Landlord shall have the right to draw on the existing Letter of Credit. To the extent Tenant is permitted under the Lease to reduce the amount of the Letter of Credit, Landlord shall cooperate with Tenant to allow the original Letter of Credit to be exchanged by the issuing bank for a replacement Letter of Credit in such lower amount.

e. Draws.

(i) Landlord may draw on, use, apply, or retain the proceeds of the Letter of Credit to the same extent that Landlord may use, apply, or retain the cash security deposit, as set forth in Section 34 of the Lease;

(ii) Landlord may draw on the Letter of Credit, in whole or in part, from time to time, at Landlord's election, as and when Landlord has the right to make draws on the Security Deposit pursuant to Section 34; and

(iii) If Landlord partially draws down the Letter of Credit, Tenant shall, within ten (10) business days after Landlord gives Tenant notice thereof, restore all amounts drawn by Landlord, or substitute cash security instead.

f. Cooperation by Tenant. Tenant hereby agrees to cooperate, at its expense, with Landlord to promptly execute and deliver to Landlord any and all modifications, amendments, and replacements of the Letter of Credit, as Landlord may reasonably request to carry out the terms and conditions of Section 34.

EXHIBIT "H"

EXPANSION SPACE

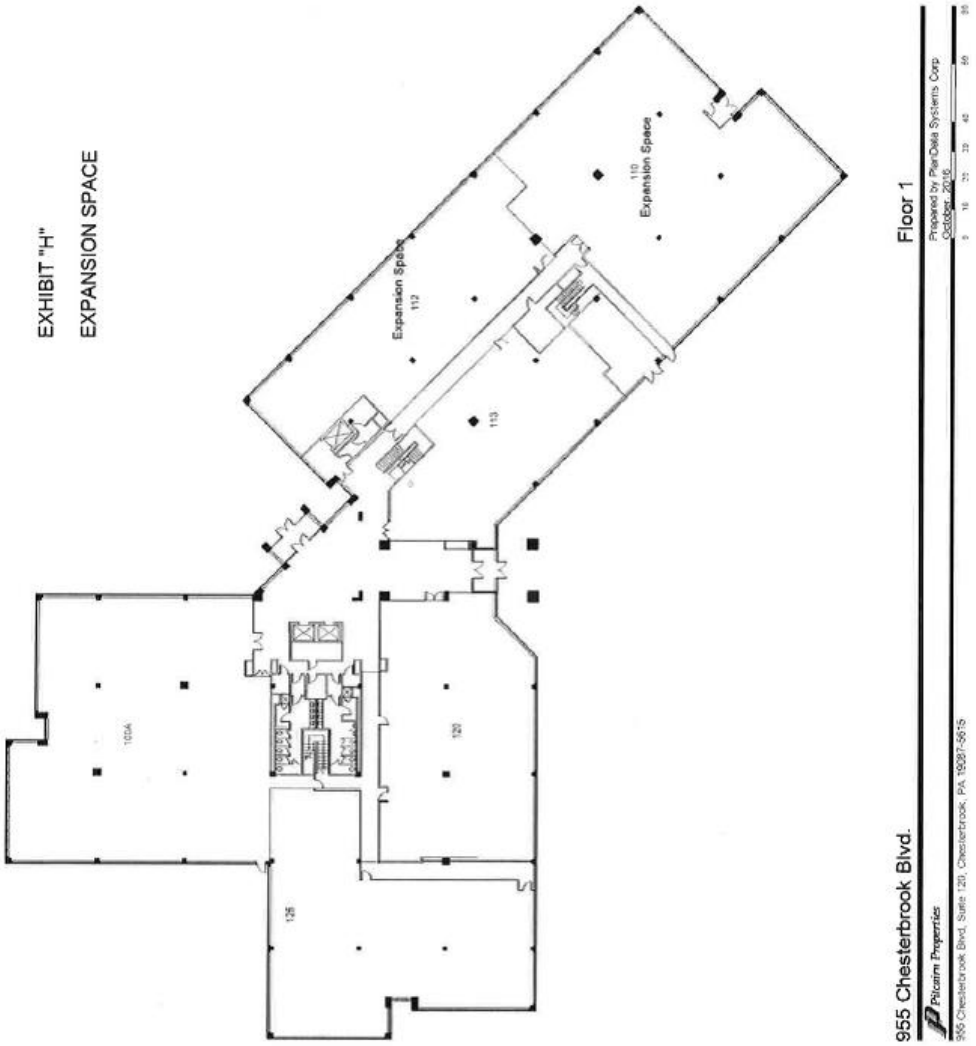


EXHIBIT "I"

RFO SPACE

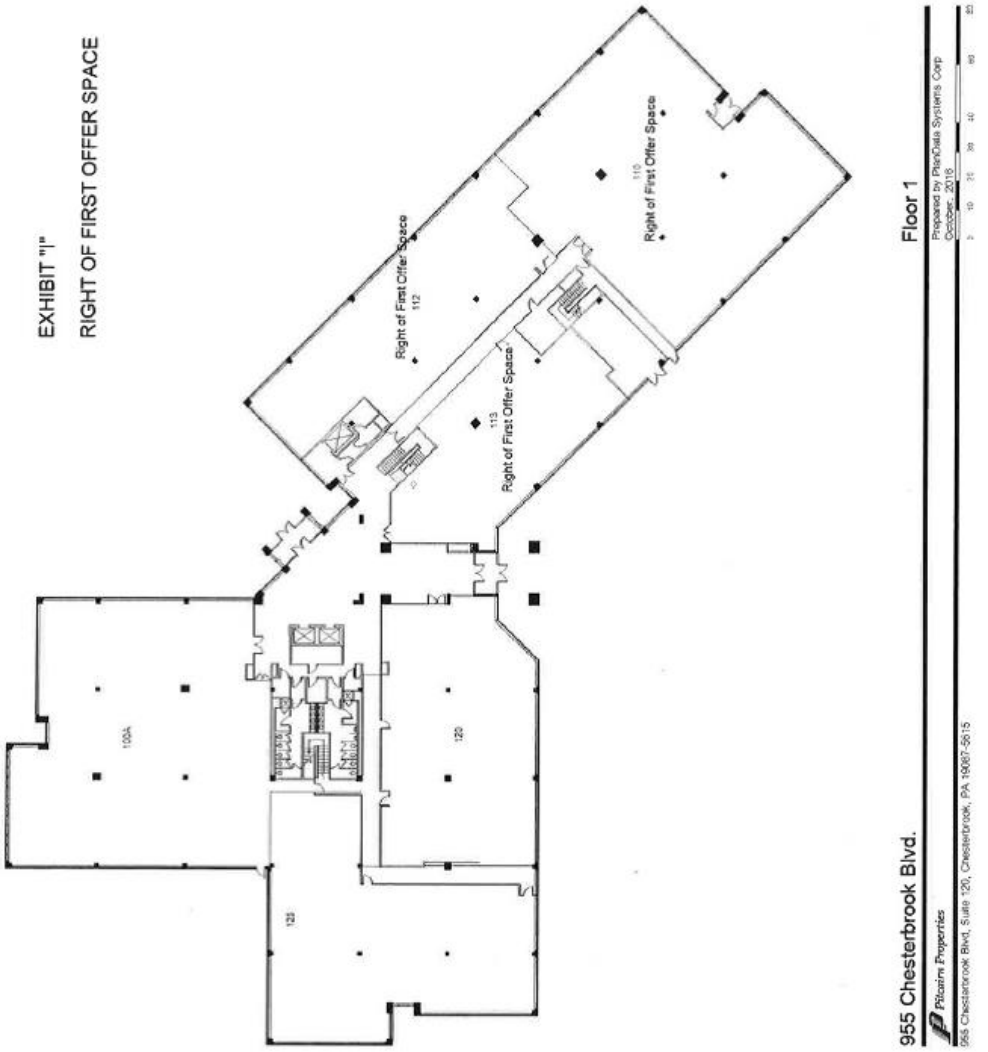
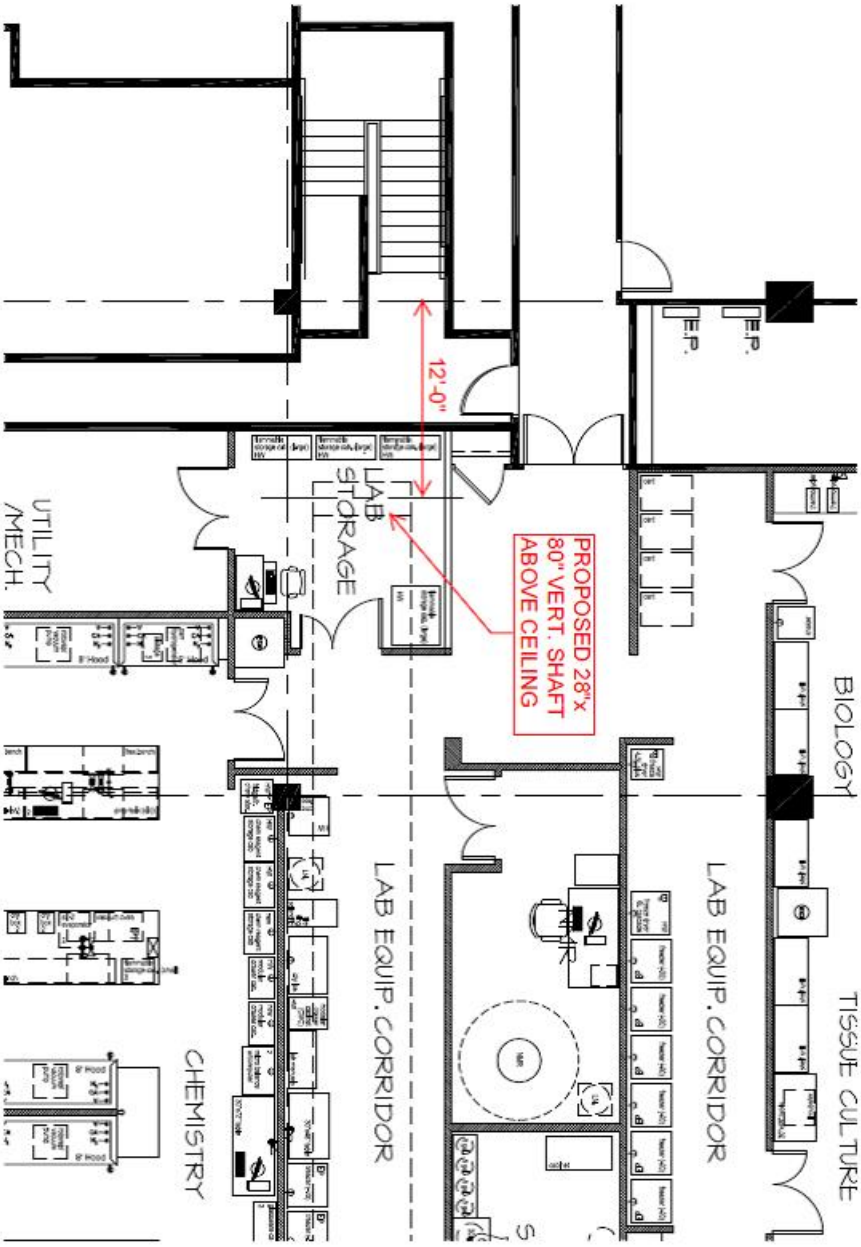
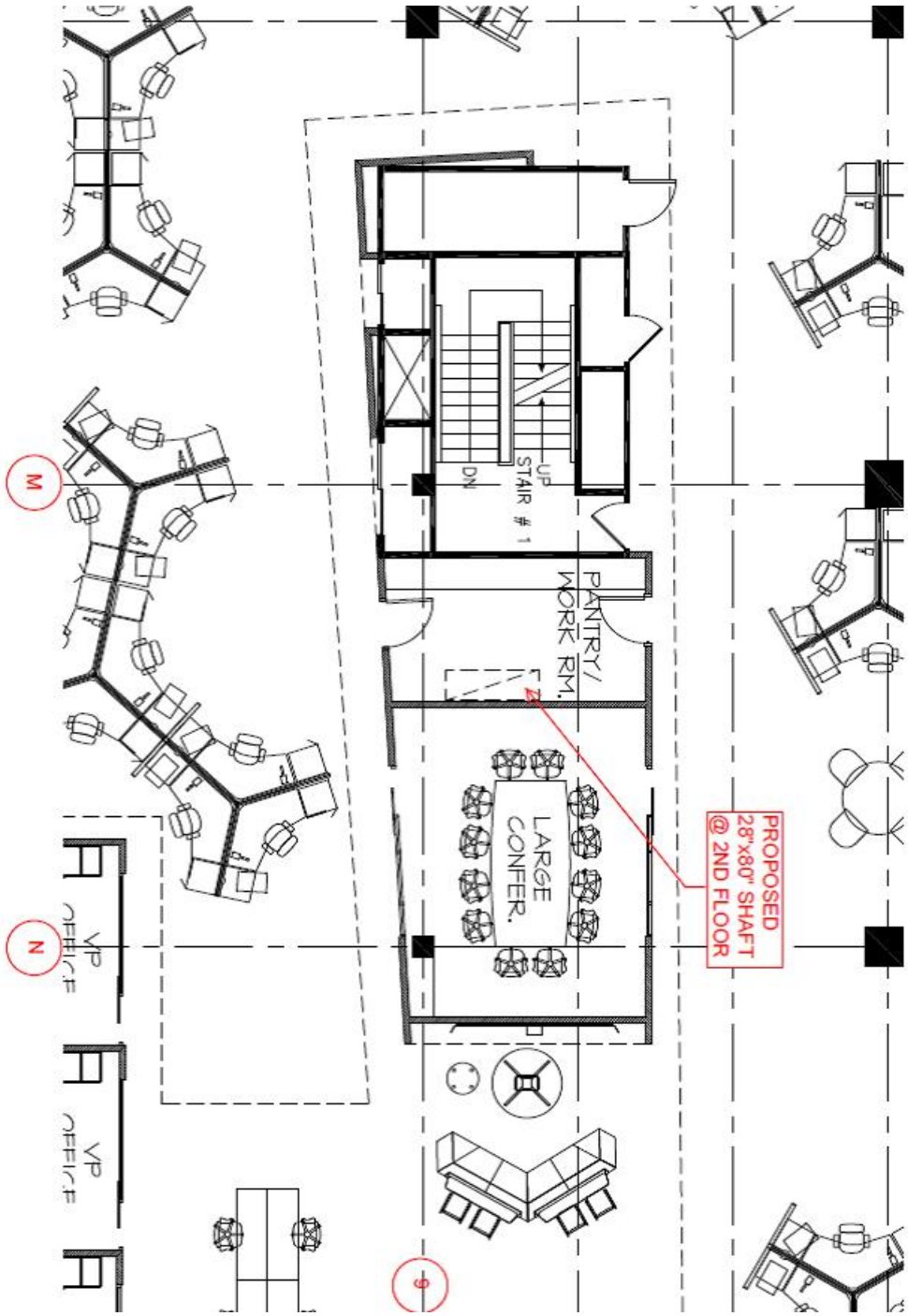
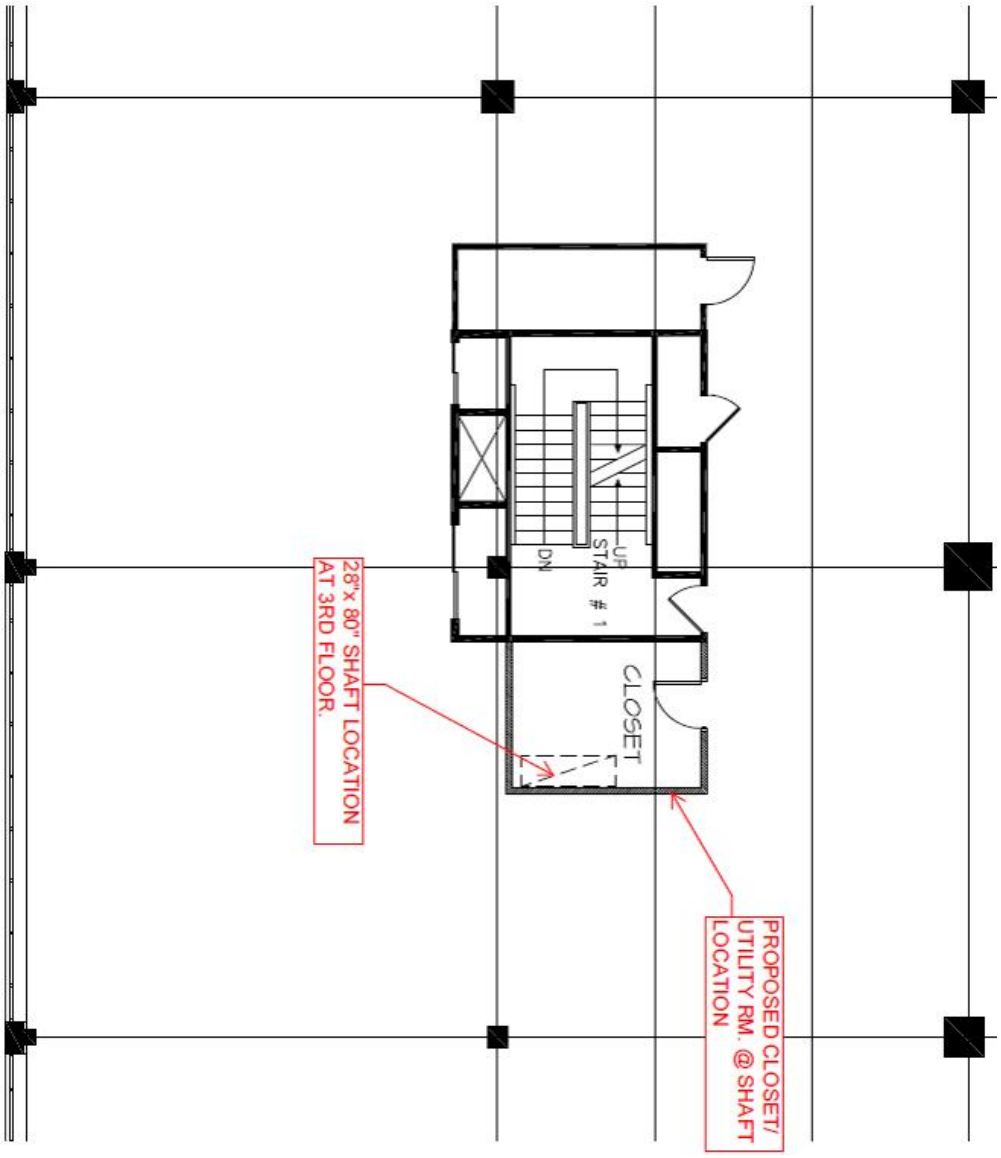


EXHIBIT "J"

VENTILATION DUCT LOCATION




M
N
UP
STAIR # 1
DN
PANTRY/
WORK RM.
LARGE
CONFER.
PROPOSED
28"x80" SHAFT
@ 2ND FLOOR
VP
OFFICE
VP
OFFICE


UP
STAIR # 1
DN
CLOSET
28"x 80" SHAFT LOCATION
AT 3RD FLOOR.
PROPOSED CLOSET/
UTILITY RM. @ SHAFT
LOCATION

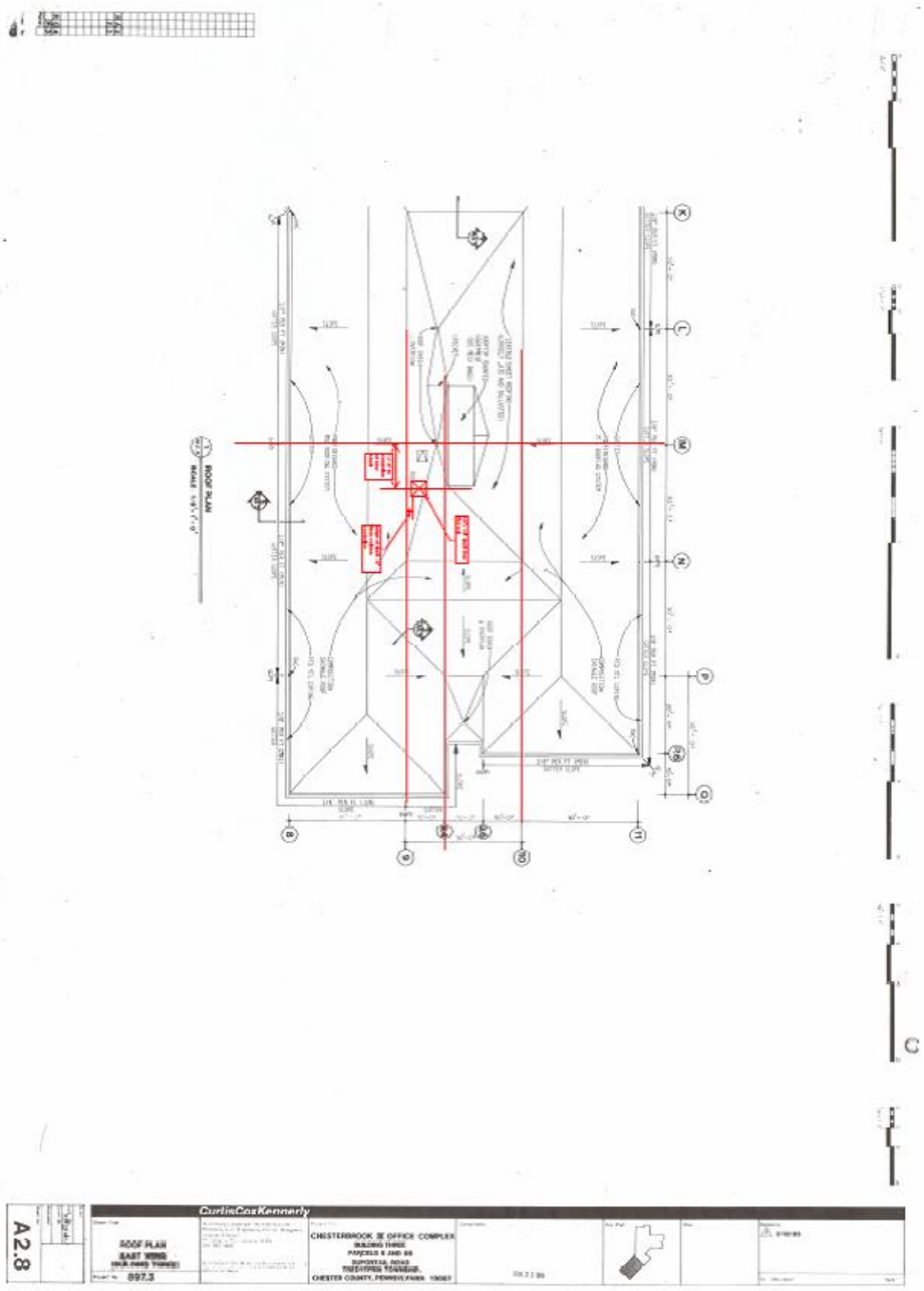

ROOF PLAN
A2.8
CurtisCoxKennerly
ROOF PLAN
EAST WING
897.3
CHESTERBROOK 3E OFFICE COMPLEX
BUILDING THREE
PARCELS 6 AND 6B
DUPORTAIL ROAD
TREDYFFRIN TOWNSHIP,
CHESTER COUNTY, PENNSYLVANIA 19087

EXHIBIT "K"

GENERATOR AND AHU LOCATIONS

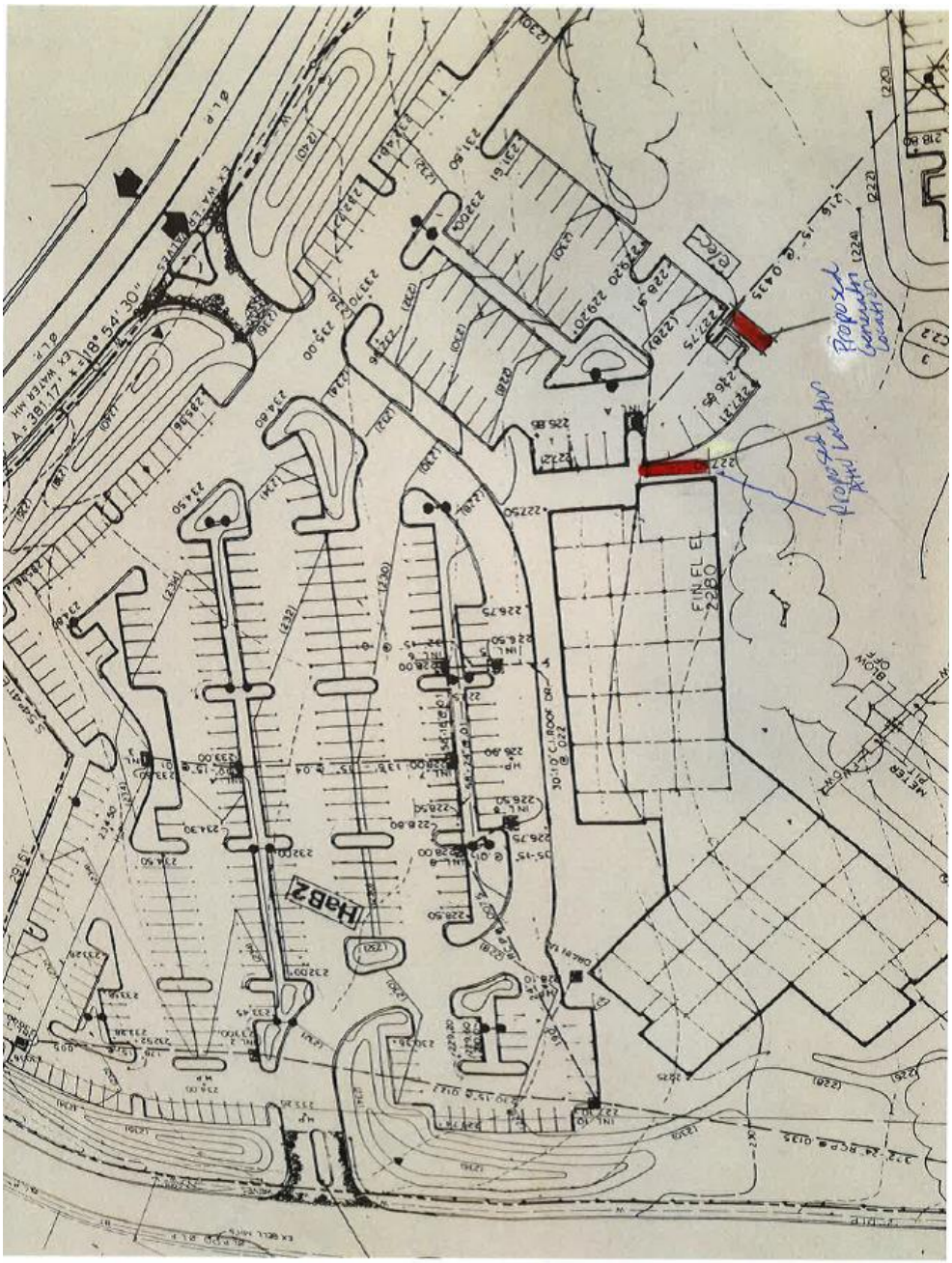


EXHIBIT "L"

FORM OF LANDLORD WAIVER

Form of Consent to Removal of Personal Property

As of December __, 2016, the undersigned, Chesterbrook Partners, L.P., a Delaware limited partnership, ("Lessor"), under the terms of a lease, as amended, a copy of which is attached hereto (the "Lease"), acknowledges that, TREVENA, INC., a Delaware corporation ("Lessee"), has entered into a Loan and Security Agreement dated September 19, 2014 (as amended, restated, supplemented or otherwise modified from time to time, the "Security Agreement"), with OXFORD FINANCE LLC as Collateral Agent ("Oxford" and in such capacity, "Collateral Agent"), the lenders a party thereto from time to time including Oxford in its capacity as a Lender (each a "Lender" and collectively, the "Lenders") under the terms of which Collateral Agent is granted a security interest, for the ratable benefit of the Lenders, in substantially all of Lessee's assets and properties, including all inventory and equipment including all tangible property now owned or hereafter acquired. Any reference herein to the "demised premises" shall mean the premises leased to Lessee pursuant to the Lease.

Notices If the Lease has terminated as a result of an event of default thereunder, Lessor will provide Collateral Agent notice of such termination, and Lessor will permit Collateral Agent a total of thirty (30) days from the time that Collateral Agent first receives the notice to commence to exercise its rights under "Limited Right of Entry" below. Lessor agrees not to dispose of any of Lessee's Property (as defined below) nor assert any right or interest therein unless Collateral Agent has first received such notice and been permitted thirty (30) days to exercise its rights in and to Lessee's Property. If Lessor shall not have provided Collateral Agent the notice, Collateral Agent will provide Lessor notice in writing to 955 Chesterbrook Boulevard, Suite 120, Wayne, PA 19087 not less than two (2) Business Days prior to entry of the Collateral Agent's intention to enter the demised premises for the purpose of exercising Collateral Agent's remedies as a secured creditor following the occurrence of an Event of Default (as defined in the Security Agreement).

Subordination Lessor hereby subordinates to Collateral Agent any lien, security interest or right that Lessor may have against the personal property or trade fixtures or equipment or goods now or hereafter situated in the demised premises belonging to Lessee (collectively, "Lessee's Property").

Limited Right of Entry Lessor acknowledges that, following the giving of the applicable notice set forth in the "Notices" section, Collateral Agent or its agent or representative shall have the limited right to enter into and remain in possession of the demised premises for a reasonable period, which period of entry and possession (a) shall not to exceed thirty (30) consecutive days (the "Entry Period") and (b) shall not extend beyond the earlier of (i) thirty (30) days following the notice given by Lessor to Collateral Agent under "Notices" above or (ii) the expiration date of the Lease in accordance with its terms. The sole purpose of the right of entry and possession during the Entry Period shall be for the purpose of enforcing its liens and security interests in Lessee's Property, including the sale or removal from the demised premises of Lessee's

Property, provided no sale or auction shall be held at the demised premises or any portion of Chesterbrook Corporate Center®. Collateral Agent agrees, at Collateral Agent's cost and expense, to promptly repair, or promptly reimburse Lessor for the reasonable costs of repair of any actual damage occasioned by Collateral Agent or its agent or representative in connection with its entry, removal and access described herein, provided that Collateral Agent shall not be responsible for repairs beyond restoring (i) the office portion of the demised premises to substantially the same condition as prior to Collateral Agent's or its agent's or representative's entry, removal and access, and (ii) the laboratory portion of the demised premises to substantially the same condition that is commercially reasonable for marketing purposes (e.g., patching of walls and floors, no exposed ceiling beams); provided, however, in no event shall Collateral Agent have any obligation to repair, or reimburse Lessor for, damages resulting from any act or failure to act by Lessee. Collateral Agent shall pay to Lessor, on a weekly basis in advance (pro rata, depending on the number of days Collateral Agent is in possession), the amount equal to the current monthly rent accruing under the Lease during the period while Collateral Agent is in possession of the demised premises; provided, however, (i) such rent shall not include any rent in arrears or default, or holdover rate increases, and provided that in no event shall Collateral Agent be obligated to pay rent for any period to the extent Lessee has paid rent for such period and (ii) Collateral Agent shall not assume or be deemed to have assumed any obligations of Lessee under such Lease and shall not incur any liabilities or obligations whatsoever with respect to the Lease other than the payments and obligations described in this Agreement. To the extent that a contractor of Collateral Agent or its agent or representative shall enter upon the demised premises pursuant to the authority granted under this agreement to inspect or remove Lessee's Property, Collateral Agent shall maintain or cause its contractor, agent or representative to maintain comprehensive general liability insurance coverage, blanket contractual liability, products and completed operations liability naming Landlord, its property manager and any mortgagee as additional insureds, in an amount per occurrence of not less than Two Million ($2,000,000.00) Dollars combined single limit bodily injury and property damage. Lessee and Collateral Agent hereby acknowledge that if Collateral Agent elects not to remove all of Lessee's Property during the aforementioned Entry Period, then Lessee's Property shall be deemed abandoned and Lessor may remove and store any remaining items of Lessee's Property at Lessee's expense or otherwise dispose of same in a manner to be determined in Lessor's good faith discretion in accordance with applicable law.

No Assumption and Limitation of Lessor's Acknowledgment and Subordination Lessor further agrees that Collateral Agent's rights have been given for security purposes only, and that unless and until Collateral Agent agrees expressly and in writing to do so, Collateral Agent shall have no obligations whatsoever under the Lease except as otherwise provided above. This subordination and waiver of Lessor's lien is not limited to the specific Security Agreement described hereinabove and will apply to any and all other loans, indebtednesses, or security interests in favor of Collateral Agent whether or not expressly described herein; provided, however, the subordination of Lessor's liens hereunder to the liens and security interests of Lender are limited to liens and security interests of Lender in Lessee's Property to the extent they secure indebtedness in an outstanding amount that is less or equal to Fifty Million Dollars ($50,000,000.00).

Indemnification. Collateral Agent hereby agrees to indemnify and hold harmless Lessor and its directors, officers, employees, and affiliates (each of the foregoing entities, an "Indemnified Person") in connection with any actual, out-of-pocket losses, claims, damages, liabilities, or

other expenses (including reasonable legal or other expenses incurred in connection with investigating, defending, or participating in any such loss, claim, damage, liability, or action or other proceeding) to which such Indemnified Persons may become subject, insofar as such losses, claims, damages, liabilities or other expenses (or actions or other proceedings commenced or threatened in respect thereof) result from breach by Collateral Agent of this agreement or actions or omissions of Collateral Agent in exercising its rights described herein, excluding losses, claims, damages, liabilities or other expenses to the extent caused by any such Indemnified Person's negligence, willful misconduct or breach of this Agreement.

No Consequential Damages. Notwithstanding anything to the contrary set forth herein, in no event shall either Lessor or Collateral Agent be liable to the other or any other person for any special, consequential, exemplary damages or lost profits or diminution in value of the demised premises.

Miscellaneous This agreement shall be binding upon, and shall inure to the benefit of, any heirs, successors and assigns of the undersigned. This agreement is governed by the laws of the Commonwealth of Pennsylvania, without regard to the conflict of laws provisions.

[*Balance of page intentionally left blank*]

ADDRESS OF DEMISED PREMISES:

955 Chesterbrook Boulevard

Suites 110 & 200
Wayne, PA 19087

ADDRESS OF LESSOR:
955 Chesterbrook Boulevard
Suite 120
Wayne, PA 19087

ADDRESS OF OXFORD FINANCE LLC:

Oxford Finance LLC
133 N. Fairfax Street
Alexandria, VA 22314
Attn: Legal Department

CURRENT ADDRESS OF LESSEE:

Trevena, Inc.

1018 West 8th Avenue, Suite A
King of Prussia, PA 19406

LESSOR: CHESTERBROOK PARTNERS, LP

By: Tredyffrin GP, a Delaware limited liability company, its general partner

By: /s/ Mark Pasierb
Name: Mark Pasierb
Title: President

COLLATERAL AGENT: OXFORD FINANCE LLC

By: _____
Name: _____
Title: _____

LESSEE: TREVENA, INC.

By: /s/ John M. Limongelli
Name: John M. Limongelli
Title: SVP, General Counsel & Chief Administrative Officer

Exhibit 12.1

TREVENA, INC.

COMPUTATION OF RATIO OF EARNINGS TO FIXED CHARGES

	2012	2013	2014	2015	2016
			(in thousands)		
Determination of earnings					
Income/(loss) before income taxes	$ (15,636)	$ (23,251)	$ (49,701)	$ (50,528)	$ (102,994)
Add:					
Fixed Charges	340	303	234	531	1,927
Total Earnings/(loss)	(15,296)	(22,948)	(49,467)	(49,997)	(101,067)
Fixed charges:					
Interest expense and amortization of debt discount and deferred financing costs	194	150	71	334	1,738
Estimated interest component of rent expense	146	153	163	197	189
Total fixed charges	340	303	234	531	1,927
Ratio of earnings to fixed charges(1)					
Deficiency of earnings to cover fixed charges	$ 15,636	$ 23,251	$ 49,701	$ 50,528	$ 102,994

(1) For all periods presented, no ratios are provided as earnings were insufficient to cover fixed charges.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-208538) and Forms S-8 (Nos. 333-193735, 333-195957, 333-201672, 333-208948, 333-215420, and 333-215421) of our report dated March 8, 2017, with respect to the financial statements of Trevena, Inc. included in this Annual Report on Form 10-K for the year ended December 31, 2016.

/s/ Ernst & Young LLP

Philadelphia, Pennsylvania
March 8, 2017

Exhibit 31.1

Certification of Principal Executive Officer of Trevena, Inc.
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Maxine Gowen, certify that:

1. I have reviewed this Annual Report on Form 10-K of Trevena, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures, and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 8, 2017

/s/ Maxine Gowen

Maxine Gowen
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

Certification of Principal Financial Officer of Trevena, Inc.
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Roberto Cuca, certify that:

1. I have reviewed this Annual Report on Form 10-K of Trevena, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures, and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 8, 2017

/s/ Roberto Cuca

Roberto Cuca
Senior Vice President and Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

Certification Of
Principal Executive Officer
Pursuant To 18 U.S.C. Section 1350,
As Adopted Pursuant To
Section 906 Of The Sarbanes-Oxley Act Of 2002

In connection with the Annual Report of Trevena, Inc. (the "Company") on Form 10-K for the year ended December 31, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Maxine Gowen, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition of the Company at the end of the period covered by the Report and results of operations of the Company for the period covered by the Report.

Date: March 8, 2017

/s/ Maxine Gowen

President and Chief Executive Officer
(Principal Executive Officer)

This certification accompanies the Report and shall not be deemed "filed" by the Company with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

Certification Of
Principal Financial Officer
Pursuant To 18 U.S.C. Section 1350,
As Adopted Pursuant To
Section 906 Of The Sarbanes-Oxley Act Of 2002

In connection with the Annual Report of Trevena, Inc. (the "Company") on Form 10-K for the year ended December 31, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Roberto Cuca, Senior Vice President and Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2) The information contained in the Report fairly presents, in all material respects, the financial condition of the Company at the end of the period covered by the Report and results of operations of the Company for the period covered by the Report.

Dated: March 8, 2017

/s/ Roberto Cuca

Chief Financial Officer and Treasurer
(Principal Financial Officer)

This certification accompanies the Report and shall not be deemed "filed" by the Company with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.