INSMED INC

FORM 10-K
(Annual Report)

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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, 2015

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 0-30739

INSMED INCORPORATED

(Exact name of registrant as specified in its charter)

Virginia	**54-1972729**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. employer identification no.)**
10 Finderne Avenue, Building 10 Bridgewater, New Jersey 08807	
(Address of principal executive offices)	**(908) 977-9900 (Registrant's telephone number including area code)**

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 $0.01 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 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 small reporting company (See the definitions of "large accelerated filer," "accelerated filer," and "small reporting company" in Rule 12b-2 of the Exchange Act). Large accelerated filer [✓] Accelerated filer [ ] Non-accelerated filer [ ] Small 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 and non-voting common equity held by non-affiliates of the registrant on June 30, 2015, was $1,491.2 million (based on the closing price for shares of the registrant's common stock as reported on the Nasdaq Global Select Market on that date). In determining this figure, the registrant has assumed solely for this purpose that all of its directors, executive officers, persons beneficially owning 10% or more of the registrant's outstanding common stock and certain other stockholders of the registrant may be considered to be affiliates. This assumption shall not be deemed conclusive as to affiliate status for this or any other purpose.

On February 1, 2016, there were 61,857,549 shares of the registrant's common stock, $0.01 par value, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for its 2016 Annual Meeting of Shareholders to be filed with the Securities and Exchange Commission no later than April 29, 2016 and to be delivered to shareholders in connection with the 2016 Annual Meeting of Shareholders, are herein incorporated by reference in Part III of this Form 10-K.

INSMED INCORPORATED

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In this Form 10-K, we use the words "Insmed Incorporated" to refer to Insmed Incorporated, a Virginia corporation, and we use the words "Company," "Insmed," "Insmed Incorporated," "we," "us" and "our" to refer to Insmed Incorporated and its consolidated subsidiaries. Insmed, ARIKAYCE, and IPLEX are trademarks of Insmed Incorporated. This Form 10-K also contains trademarks of third parties. Each trademark of another company appearing in this Form 10-K is the property of its owner.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward looking statements. "Forward-looking statements," as that term is defined in the Private Securities Litigation Reform Act of 1995, are statements that are not historical facts and involve a number of risks and uncertainties. Words herein such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," "continues," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) identify forward-looking statements.

Forward-looking statements are based upon our current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause our actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timing discussed, projected, anticipated or indicated in any forward-looking statements. Such factors include, among others, the factors discussed in Item 1A "Risk Factors" as well as those discussed in Item 7 under the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere throughout this Annual Report on Form 10-K and the following: our ability to complete development of, receive regulatory approval for, and successfully commercialize ARIKAYCE, or liposomal amikacin for inhalation (LAI), and INS1009, inhaled treprostinil prodrug; our estimates of expenses and future revenues and profitability; our plans to develop and market new products and the timing of these development programs; status, timing, and the results of preclinical studies and clinical trials and preclinical and clinical data described herein; the timing of responses to information and data requests from the US Food and Drug Administration (the "FDA"), the European Medicines Agency ("the EMA"), and other regulatory authorities; our clinical development of product candidates; our ability to obtain and maintain regulatory approval for our product candidates; our expectation as to the timing of regulatory review and approval; our estimates regarding our capital requirements and our needs for additional financing; our estimates of the size of the potential markets for our product candidates; our selection and licensing of product candidates; our ability to attract third parties with acceptable development, regulatory and commercialization expertise; the benefits to be derived from corporate license agreements and other third party efforts, including those relating to the development and commercialization of our product candidates; the degree of protection afforded to us by our intellectual property portfolio; the safety and efficacy of our product candidates; sources of revenues and anticipated revenues, including contributions from license agreements and other third party efforts for the development and commercialization of products; our ability to create an effective direct sales and marketing infrastructure for products we elect to market and sell directly; the rate and degree of market acceptance of our product candidates; the timing, scope and rate of reimbursement for our product candidates; the success of other competing therapies that may become available; and the availability of adequate supply and manufacturing capacity and quality for our product candidates.

We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the Securities and Exchange Commission, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

PART I

ITEM 1. BUSINESS

Business Overview

Insmed is a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. Our lead product candidate is ARIKAYCE™, or liposomal amikacin for inhalation (LAI), which is in late-stage development for patients with nontuberculous mycobacteria (NTM) lung disease, a rare and often chronic infection that is capable of causing irreversible lung damage and can be fatal. Our earlier stage pipeline includes INS1009, a nebulized prodrug formulation of treprostinil, a vasodilator of pulmonary arterial vascular beds. We believe INS1009 may offer a differentiated product profile with therapeutic potential in pulmonary arterial hypertension (PAH), idiopathic pulmonary fibrosis (IPF), sarcoidosis, and severe refractory asthma.

We are conducting a global phase 3 clinical study of ARIKAYCE (the 212 or CONVERT study) in adult patients with NTM lung disease caused by *Mycobacterium avium* complex (MAC), the predominant infective species in NTM lung disease in the United States (US), Europe, and Japan. The European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) is reviewing our marketing authorization application (MAA) seeking approval of ARIKAYCE for the treatment of MAC lung disease in adult patients who have persistent positive sputum cultures despite the use of medically appropriate first-line therapy. We are also advancing a phase 1 study of INS1009 in healthy subjects. In addition to INS1009, our earlier-stage pipeline includes preclinical compounds that we are evaluating in multiple rare diseases of unmet medical need, including methicillin-resistant staph aureus (MRSA), NTM, PAH and sarcoidosis. We are also evaluating additional formulations and delivery options for treprostinil, including delivery via a metered dose inhaler. To complement our internal research, we actively seek in-licensing and acquisition opportunities for a broad range of rare diseases.

The table below summarizes the current status and anticipated milestones for ARIKAYCE and INS1009.

Product Candidate/Target Indications	Status	Next Expected Milestones
ARIKAYCE for adult patients with refractory NTM lung infections caused by MAC	• We are advancing the CONVERT study, a randomized, open-label global phase 3 clinical study of ARIKAYCE in adult patients with treatment refractory NTM lung disease caused by MAC. • In late 2015, we responded to the EMA's 120-day questions, which are a standard part of the MAA evaluation process in the EU. • The US FDA has designated ARIKAYCE as an orphan drug, a breakthrough therapy and a qualified infectious disease product (QIDP). Breakthrough therapy features intensive guidance on efficient drug development and offers the potential for a rolling review. A QIDP-designated product qualifies for fast track designation and is eligible for priority review. • The Committee for Orphan Medicinal Products of the EMA has issued a positive opinion for orphan designation of ARIKAYCE.	• We expect to achieve our patient enrollment objective in the CONVERT study in the second half of 2016. • We expect to receive the CHMP's 180-day list of outstanding issues (LOI) related to our MAA in the first quarter of 2016. • We anticipate responding to the LOI and participating in an oral hearing with the CHMP in the second quarter of 2016 to address the LOI on our MAA for ARIKAYCE. We continue to expect the CHMP to render an opinion around the middle of 2016. • If approved, we expect ARIKAYCE would be the first approved inhaled antibiotic treatment specifically indicated for NTM lung infections in North America, Europe, and Japan. • If approved, we plan to commercialize ARIKAYCE in certain countries in Europe and in the US, and eventually Canada, Japan and certain other countries.
INS1009 (nebulized treprostinil prodrug) for PAH, IPF, sarcoidosis and severe refractory asthma	• In the fourth quarter of 2015 we initiated a phase 1 randomized, double-blind, placebo-controlled single ascending dose study of INS1009 for inhalation to determine its safety, tolerability, and pharmacokinetics in healthy volunteers.	• We expect to present the results of our phase 1 study of INS1009 at a future medical meeting.

Corporate History

We were incorporated in the Commonwealth of Virginia on November 29, 1999. On December 1, 2010, we completed a business combination with Transave, Inc. (Transave), a privately held, New Jersey-based company focused on the development of differentiated and innovative inhaled pharmaceuticals for the site-specific treatment of serious lung infections.

Our Strategy

Our strategy focuses on the needs of patients with rare diseases. We are currently focused on the development and commercialization of ARIKAYCE, or LAI. There are currently no inhaled products specifically indicated to treat NTM lung disease in North America, Europe or Japan. While we believe that ARIKAYCE has the potential to treat many different diseases, we are prioritizing securing regulatory approval of ARIKAYCE in NTM lung disease caused by MAC. We are also advancing earlier-stage programs in other rare disorders, including a phase 1 study of INS1009, our nebulized prodrug formulation of treprostinil.

Our current priorities are as follows:

- Enrolling the CONVERT study;
- Securing approval of ARIKAYCE in the European Union for the treatment of MAC lung disease in adult patients who have persistent positive sputum cultures despite the use of medically appropriate first-line therapy;
- Preparing our US NDA submission based on the results of the CONVERT study;
- Ensuring our product supply chain will support the clinical development and if approved, commercialization of ARIKAYCE;
- Preparing for potential commercialization of ARIKAYCE in certain countries in the EU and the US;
- Defining further research and lifecycle management strategies for ARIKAYCE, including investigator-initiated studies;
- Completing the phase 1 study of INS1009, our nebulized treprostinil prodrug, and investigating its use in multiple indications;
- Presenting preclinical findings from our earlier-stage program(s); and
- Expanding our rare disease pipeline through corporate development.

Product Pipeline

ARIKAYCE for patients with NTM lung disease

Our lead product candidate is ARIKAYCE, or LAI, a novel, once-daily formulation of amikacin that is in late-stage clinical development for patients with NTM lung disease, a rare and often chronic infection that is capable of causing irreversible lung damage and which can be fatal. Amikacin solution for parenteral administration is an established drug that is effective against a variety of NTM; however, its use is limited by the need to administer it intravenously and by toxicity to hearing, balance, and kidney function (Peloquin et al., 2004). Our advanced pulmonary liposome technology uses charge-neutral liposomes to deliver amikacin directly to the lung where it is taken up by the lung macrophages where the NTM infection resides. This prolongs the release of amikacin in the lungs while minimizing systemic exposure thereby offering the potential for decreased systemic toxicities. ARIKAYCE's ability to deliver high levels of amakacin directly to the lung distinguishes it from intravenous amakacin. ARIKAYCE is administered once-daily using an optimized, investigational eFlow® Nebulizer System manufactured by PARI Pharma GmbH, a novel, highly efficient and portable aerosol delivery system.

The CONVERT study

ARIKAYCE is currently being evaluated in a phase 3 randomized, open-label, global clinical study designed to confirm the culture conversion results seen in our phase 2 clinical trial. This phase 3 study, which is known as the CONVERT (or 212) study, is enrolling non-cystic fibrosis (non-CF) patients 18 years and older with an NTM lung infection caused by MAC that is refractory to a stable multi-drug regimen for at least six months with the regimen either ongoing or completed within 12 months of screening. In our completed phase 2 study, the subgroup of non-CF patients with NTM

lung infection caused by MAC demonstrated the greatest response to treatment with ARIKAYCE. We believe this clinical trial will confirm the culture conversions seen in the phase 2 study and provide the basis for submitting a New Drug Application (NDA) to the US Food and Drug Administration (FDA), as well as regulatory submissions in Japan and other countries.

After a screening period of approximately 10 weeks, eligible subjects will be randomized 2:1 to once-daily ARIKAYCE plus a multi-drug regimen or a multi-drug regimen without ARIKAYCE. For every two patients that are randomized to receive ARIKAYCE plus a multi-drug regimen, one patient is randomized to receive a multi-dose regimen without ARIKAYCE. The primary efficacy endpoint is the proportion of subjects who achieve culture conversion at Month 6 (defined as three consecutive negative sputum cultures collected monthly) in the ARIKAYCE plus multi-drug regimen arm compared to the arm in which subjects receive a multi-drug regimen without ARIKAYCE. The study's key secondary endpoints include the change from baseline in the six-minute walk test and off-treatment assessments to evaluate durability of effect. The study also includes a comprehensive pharmacokinetic sub-study in Japanese subjects in lieu of a separate local pharmacokinetic study in Japanese subjects.

At Month 8, after all sputum culture results are known up to and including Month 6, subjects will be assessed as converters or non-converters for the primary efficacy endpoint. A converter is defined as a patient with three consecutive monthly sputum samples at Month 6 that test negative for the presence of MAC NTM. All converters will continue on their randomized treatment regimen for 12 months beginning from the first negative culture that defined culture conversion. All converters will return for off-treatment follow-up visits. A 12-month off-treatment study visit will be the last study visit for the CONVERT study. All non-converters in the study at Month 8 will be eligible to enter a separate open-label study (the 312 study). The primary objective of the 312 study is to evaluate the long-term safety and tolerability of ARIKAYCE for up to 12 months. The secondary endpoints of the 312 study include evaluating the proportion of subjects achieving culture conversion (three consecutive negative sputum cultures without relapse or recurrence) by Month 6 and the proportion of subjects achieving culture conversion by Month 12 (end of treatment).

The protocol for the CONVERT study incorporates feedback from the FDA and the EMA via its scientific advice working party process, as well as local health authorities, including Japan's Pharmaceuticals and Medical Devices Agency, and was approved in the US by a central Institutional Review Board (IRB). We initiated the global trial in early 2015 and expect to complete patient enrollment in the second half of 2016. If the CONVERT study meets the primary endpoint of culture conversion at Month 6, we believe we would be eligible to submit an NDA pursuant to 21 CFR 314 Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses), which permits FDA to approve a drug based on a "surrogate endpoint" provided the sponsor commits to study the drug further to verify and describe the drug's clinical benefit. We believe that efficacy data from the CONVERT study after Month 6 will suffice to meet this commitment. We are currently conducting CONVERT at over 115 sites in the US, Europe, Australia, New Zealand, Asia and Canada. The CONVERT study is designed to enroll enough subjects to ensure at least 261 subjects are evaluable for the primary endpoint at Month 6.

Phase 2 study (the 112 study)

Our completed phase 2 study, which is also known as the 112 study, was a randomized, double-blind, placebo-controlled study that evaluated the efficacy and safety of ARIKAYCE in adults with NTM lung disease due to MAC or *Mycobacterium abscessus* (*M. abscessus*) that was refractory to guideline-based therapy. The study included an 84-day double-blind phase in which subjects were randomized 1:1 either to ARIKAYCE once-daily plus a multi-drug regimen or to placebo once-daily plus a multi-drug regimen. After completing the 84-day double-blind phase, subjects had the option of continuing in an 84-day open-label phase during which all subjects received ARIKAYCE plus a

multi-drug regimen. The study also included 28-day and 12-month off-ARIKAYCE follow-up assessments to evaluate safety and durability of effect.

Eighty-nine subjects were randomized and dosed in the study. Of the 80 subjects who completed the 84-day double-blind phase, 78 subjects elected to continue in the open-label phase and received ARIKAYCE plus a multi-drug regimen for an additional 84 days. Seventy-six (76) percent (59/78) of subjects who elected to continue in the open-label phase of the study completed the open-label study.

The primary efficacy endpoint of the study was the change from baseline (day 1) to the end of the double-blind phase of the trial (day 84) in a semi-quantitative measurement of mycobacterial density on a seven-point scale. ARIKAYCE did not meet the pre-specified level for statistical significance although there was a positive trend (p=0.072) in favor of ARIKAYCE. The p-value for the key secondary endpoint of culture conversion to negative at Day 84 was 0.003, in favor of ARIKAYCE.

After establishing the primary endpoint for the phase 3 CONVERT study, we explored the microbiologic outcomes from the 112 study using the more stringent definition of culture conversion, which is defined as at least three consecutive monthly sputum samples that test negative for NTM bacteria. This definition of culture conversion is in the American Thoracic Society/Infectious Disease Society of America (ATS/IDSA) Guidelines (Griffith et al. 2007) and used in clinical practice. The preliminary results of these analyses are summarized below:

- Twenty subjects who received ARIKAYCE in the 112 study achieved culture conversion status over the 168-day treatment phase (13 received ARIKAYCE in the double-blind phase and seven received ARIKAYCE in the open-label phase).
- Three additional subjects who started ARIKAYCE in the open-label phase achieved culture conversion by the 28-day off-ARIKAYCE follow-up assessment.

The 112 study included a 12-month off-ARIKAYCE follow up visit in order to collect sputum culture results. These results were collected and analyzed to assess the durability of the ARIKAYCE treatment effect for both the group of subjects who achieved culture conversion and the group of subjects who did not achieve culture conversion during the 168-day treatment phase. The preliminary results of these analyses are summarized below:

- Seventeen of the total 23 subjects who achieved culture conversion during the study attended their 12-month off-ARIKAYCE follow-up visit. The NTM sputum culture results for these 17 subjects are as follows:
    - Eleven subjects remained culture negative; nine of these subjects were non-CF subjects with MAC (eight of these nine subjects were off all NTM treatments at this time) and two were subjects with non-CF *M. abscessus* at the time of study entry (both subjects were continuing treatment for *M. abscessus*).
    - Three non-CF subjects with MAC could not produce sputum despite reasonable attempts. These same subjects were off all NTM treatments at this time. This is consistent with the achievement of treatment success during the follow-up period as the lack of sputum production is indicative of symptom resolution.
    - Two non-CF subjects with MAC were broth culture positive only, which may represent contamination (a false positive) or a new infection rather than a relapse.
    - One non-CF subject with *M. abscessus* was also broth culture positive only.

- Twenty eight of the subjects who did not achieve culture conversion during the 168-day treatment phase of the study provided sputum at the 12-month follow up visit, of which 22

subjects continued to have positive sputum cultures with six subjects showing a negative culture, with approximately 50% of subjects continuing on NTM treatment.

Eligibility for the 112 study required subjects to have been on ATS/IDSA Guideline therapy for at least six months prior to screening and to have had persistently positive sputum mycobacterial cultures.

During the double-blind phase, the majority of the subjects in both treatment groups experienced at least one treatment-emergent adverse event (TEAE). All of the most common TEAEs, except diarrhea, occurred more frequently in the ARIKAYCE group than in the placebo group. Renal TEAEs were reported infrequently. Audiovestibular TEAEs were reported in similar proportions of subjects in the two treatment groups in the double-blind phase and were reported infrequently in the open-label phase. TEAEs considered related by the investigator were reported more frequently in the ARIKAYCE group than in the placebo group in the double-blind phase (ARIKAYCE: 72.7%, placebo: 37.8%). However, in the open-label phase, the overall incidence of treatment-related adverse events was lower in the group of subjects who had received ARIKAYCE during the double-blind phase of the trial than in the group of subjects who had received placebo during the double-blind phase of the trial (ARIKAYCE: 48.6%, placebo: 60.5%).

One subject died during the double-blind phase of pneumonia and acute respiratory distress syndrome and one subject died during the open-label phase of multi-organ failure, intestinal ischemia, and urosepsis. None of the events in either subject were considered to be related to the study drug by the investigator. All of these events were assessed by the Data Monitoring Committee, with no change in their assessment of the risk benefit of ARIKAYCE. In the double-blind phase, serious adverse events were reported for a greater proportion of subjects in the ARIKAYCE group than in the placebo group (18.2% versus 8.9%, respectively). In the double-blind phase, a greater proportion of subjects in the ARIKAYCE treatment group than in the placebo group reported adverse events leading to study drug discontinuation (ARIKAYCE: 18.2%; placebo: 0%). The most commonly reported TEAEs leading to study drug discontinuation in the ARIKAYCE group were infective exacerbation of underlying bronchiectasis (6.8%) and dyspnea (4.5%). The incidence of adverse events leading to discontinuation did not increase in the ARIKAYCE group with longer exposure to the study drug in the open-label phase compared with the double-blind phase (17.1% and 18.2%, respectively). In the open-label phase, 27.9% of subjects who had received placebo during the double-blind phase of the trial reported adverse events leading to study drug discontinuation.

No clinically significant changes in laboratory values, vital signs, BMI, and pulmonary function tests were observed over the course of the study. The results discussed above are preliminary findings based on currently available data.

MAA for NTM

We are currently seeking EU approval of ARIKAYCE for the treatment of NTM lung disease caused by MAC in adult patients who have persistent positive sputum cultures despite the use of medically appropriate first-line therapy. Our MAA filing is based on data from the 112 study. We submitted our responses to the CHMP's 120-day questions in December 2015. We expect to receive the CHMP's 180-day LOI in the first quarter of 2016. We anticipate responding to the LOI and participating in an oral hearing with the CHMP in the second quarter of 2016 to address the LOI on our MAA for ARIKAYCE. The 120-day and 180-day communications are part of CHMPs official review timetable. We expect the CHMP to render an opinion on our MAA around the middle of 2016.

We initially filed our MAA with the EMA seeking approval of ARIKAYCE in the EU for the treatment of NTM lung infections as well as *Pseudomonas* lung infections in CF patients. In the third

quarter of 2015, the CHMP adopted our request to withdraw the *Pseudomonas* indication from our MAA. We chose to withdraw the *Pseudomonas* indication after receiving a request from EMA for additional information with respect to the similarity of ARIKAYCE to the TobiPodhaler given this product's orphan designation. While it is our view that ARIKAYCE is not similar to the TobiPodhaler, a comprehensive response to the EMA's request would have required us to divert significant resources from and potentially delay the regulatory advancement of the NTM indication. Given the significant need for approved medications for patients with NTM lung disease, we concluded the most appropriate near-term course of action for ARIKAYCE was to focus exclusively on advancing the regulatory review process for the NTM indication.

NTM Market Opportunity

NTM is a rare and serious disorder associated with increased morbidity and mortality. There is an increasing rate of lung disease caused by NTM and this is an emerging public health concern worldwide. Patients with NTM lung disease may experience a multitude of symptoms such as fever, weight loss, cough, lack of appetite, night sweats, blood in the sputum, and fatigue. Patients with NTM lung disease frequently require lengthy hospital stays to manage their condition. There are no products specifically indicated for the treatment of NTM lung disease in the US, Europe and Canada. Current guideline-based approaches involve multi-drug regimens that may cause severe side effects and treatment can be as long as two years or more.

The prevalence of human disease attributable to NTM has increased over the past two decades. In a decade-long study (1997-2007), researchers found that the prevalence of NTM in the US is increasing at approximately 8% per year and that NTM patients on Medicare over the age of 65 are 40% more likely to die over the period of the study than those who did not have the disease (Adjemian et al., 2012). A 2015 publication from co-authors from several US government departments stated that prior year statistics led to a projected 181,037 national annual cases in 2014 costing the US healthcare system approximately $1.7 billion (Strollo et al., 2015).

Our market research indicates that there are approximately 100,000 patients in the US, the EU5 (France, Germany, Italy, Spain and the United Kingdom), and Japan who have a confirmed diagnosis of NTM lung disease, of which an estimated 10 to 30 percent are refractory to current treatments. In 2012, in collaboration with the NIH, we funded a study performed by Clarity Pharma Research that showed there were an estimated 50,000 cases of pulmonary disease attributable to NTM in the US in 2011 and that such cases were estimated to be growing at a rate of 10% per year. In 2013, we engaged Clarity Pharma Research to perform a similar chart audit study of NTM in Europe and Japan. Based on results of this study, researchers estimated that there are approximately 20,000 cases of pulmonary disease attributable to NTM within the EU5 and approximately 30,000 in the 28 countries comprising the EU. In addition, there are nearly 32,000 cases in Japan. Although population-based data on the epidemiology of NTM infections in Europe are limited, consistent with US prevalence trends, recent published studies concur that prevalence in Europe is increasing and, according to a study published in the Japanese journal Kekkaku in 2011, Japan has one of the world's highest NTM disease rates.

NTM currently includes over 150 species. MAC is the predominant pathogenic species in NTM pulmonary disease in the US, Japan and Europe, followed by *M. abscessus* . Thus far, we have studied ARIKAYCE in both MAC and *M. abscessus* .

We are studying the economic and societal implications of NTM lung infections. We have conducted a burden of illness study in the US with a major medical benefits provider. This study showed that patients with NTM lung infections are costly to healthcare plans and ATS/IDSA guideline-based treatment results in healthcare savings as opposed to suboptimal treatment.

In partnership with one of the nation's largest Medicare insurance providers, we recently presented the results of three claims-based studies.

- At the Interscience Conference of Antimicrobial Agents and Chemotherapy in September 2015 researchers reported a 36.1% increase ($p<0.001$) in the incidence of NTM infections between 2008 and 2013 with the greatest incidence (56.3%) for those members 65 to 74 years of age. Following diagnosis with NTM infection, over 50% of members were still in the plan after six years (Abraham et al.).
- At Infectious Disease Week in October 2015 researchers reported that patients with NTM are using significantly greater healthcare resources in the period preceding their diagnosis. Ordering mycobacterial testing of sputum earlier may help in preventing a misdiagnosis or delaying a diagnosis (Holt et al.).
- At the Academy of Managed Care Pharmacy conference in October 2015, researchers reported significantly higher resource utilization and cost patterns for patients with NTM lung infections than their matched controls both pre- and post-diagnosis. Patients who received optimal treatment based on the 2007 ATS/IDSA guidelines showed lower healthcare resource utilization and total medical costs than patients who received suboptimal treatment. These data suggest that healthcare plans should consider mechanisms to identify and appropriately treat patients with NTM lung disease (Abraham et al.).

We plan to repeat this type of research globally in support of our overall disease awareness and education efforts.

The FDA has designated ARIKAYCE as an orphan drug, a breakthrough therapy, and a QIDP for NTM lung disease. Orphan designation features seven years of post-approval market exclusivity and QIDP features an additional five years of post-approval exclusivity. A QIDP-designated product is eligible for fast track and priority review designations. A priority review designation for a drug that is not a new molecular entity (NME) means the FDA's goal is to take action on the NDA within six months of the FDA's accepting the application as filed compared to 10 months under a standard review.

INS1009

INS1009 is an investigational sustained-release nebulized treprostinil prodrug that has the potential to address certain of the current limitations of existing inhaled prostanoid therapies. We believe that INS1009 prolongs duration of effect and may provide greater consistency in pulmonary arterial pressure reduction over time. Current inhaled prostanoid therapies must be dosed four to nine times per day for the treatment of PAH. Reducing dose frequency has the potential to ease patient burden and improve compliance. Additionally, we believe that INS1009 over time may reduce side effects, including elevated heart rate, low blood pressure, and severity and/or frequency of cough, associated with high initial drug levels and local upper airway exposure when using current inhaled prostanoid therapies. We believe INS1009 may have therapeutic potential in PAH, IPF, sarcoidosis, and severe refractory asthma.

In late 2014, we had a pre-investigational new drug (pre-IND) meeting with the FDA for INS1009 and clarified that, subject to final review of the preclinical data, INS1009 could be eligible for an approval pathway under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) ("505(b)(2) approval"). Like a traditional NDA that is submitted under Section 505(b)(1) of the FDCA, a 505(b)(2) NDA must establish that the drug is safe and effective, but unlike a traditional NDA the applicant may rely at least in part on studies not conducted by or for the applicant and for which the applicant does not have a right of reference. The ability to rely on existing third-party data to support safety and/or effectiveness can reduce the time and cost associated with traditional NDAs.

In the fourth quarter of 2015 we submitted an IND application and subsequently commenced a phase 1 study of INS1009. The phase 1 study is a randomized, double-blind, placebo-controlled single ascending dose study of INS1009 for inhalation to determine its safety, tolerability, and pharmacokinetics in healthy volunteers.

We believe INS1009 may have therapeutic potential in PAH, IPF, sarcoidosis, and severe refractory asthma.

PAH

There is no cure for PAH. PAH is a serious, progressive rare disease affecting approximately 100,000 patients globally, including approximately 25,000 treated patients in the US (Yang et al., 2006; Peacock et al. 2007; and Humbert et al. 2006). PAH ultimately leads to heart failure and the disease has a 15% one-year mortality rate (Kane et al., 2011). Several medications are used to treat PAH:

- Non-specific treatments such as anticoagulants, diuretics, and oxygen may be used. These drugs are not specifically approved for the treatment of PAH, but are commonly utilized. In specific circumstances, drugs such as digoxin or calcium channel blockers may also be used to treat PAH.
- Several drugs are approved specifically for the treatment of PAH. These drugs address three target pathophysiologic pathways: the endothelin pathway; the nitric oxide pathway; and the prostacyclin pathway. They may be used alone or in combination.

IPF

Idiopathic Pulmonary Fibrosis (IPF) is a rare, chronic, progressive, interstitial lung disease of unknown etiology that affects around five million patients worldwide. Patients with IPF are generally middle-aged or older at the time of diagnosis. Disease progression is variable but progressive fibrosis (scarring) leads ultimately to death, with a median survival of three to five years after diagnosis. Symptoms often include shortness of breath, dry cough, unintended weight loss, fatigue, and clubbing of the fingers and toes. Over time, IPF can lead to a debilitating loss of physical ability. The prevalence of IPF in the US ranges from between 90,000 and 190,000 patients, a range similar to that reported in Europe (Lee et al., 2014).

Sarcoidosis

Sarcoidosis is a granulomatous inflammatory disease that is induced by unknown antigen(s) in a genetically susceptible host (Mortaz et al. 2014). This rare, chronic systemic disease most commonly affects the lung. Several features of sarcoidosis tend to obscure the diagnosis, leading to an under-appreciation of the potential impact of the disease on the health care system and society as a whole. Sarcoidosis frequently presents with non-specific complaints, ranging from fatigue and depression, "asthma symptoms" (wheezing, cough), to arthritis and muscle pain or weakness. As such, sarcoidosis can mimic other diseases, leading to misdiagnosis and inappropriate treatments. The prevalence of sarcoidosis in the US is unknown, with estimates ranging widely from one to 40 per 100,000 (Erdal et al. 2012).

Severe refractory asthma

Severe refractory asthma is characterized by a difficulty to achieve disease control despite high-intensity treatment. Prevalence figures of severe refractory asthma are lacking, whereas longstanding estimates vary between five and 10% of all asthmatic patients. To make a reliable estimate of the prevalence of severe refractory asthma as defined by the Innovative Medicine Initiative consensus, Hekking et al. analyzed prescription data from 65 Dutch pharmacy databases, representing 500,500 adult inhabitants. Of asthmatic adults, 3.6% qualified for a diagnosis of severe refractory asthma; therefore, the prevalence of severe refractory asthma might be lower than estimated by expert opinion, which implies that currently recognized severe asthma phenotypes could meet the criteria of rare disease. (Hekking et al. October 2014).

Research and Development

Research and development expenses consist primarily of salaries, benefits and other related costs, including stock-based compensation, for personnel serving in our research and development functions. Expenses also include other internal operating expenses, the cost of manufacturing our drug candidate for clinical study, the cost of conducting clinical studies, and the cost of conducting preclinical and research activities. Our expenses related to manufacturing our drug candidate for clinical study are primarily related to activities at contract manufacturing organizations that manufacture ARIKAYCE for our use. Our expenses related to clinical trials are primarily related to activities at contract research organizations that conduct and manage clinical trials on our behalf. We incurred approximately $74.3 million, $56.3 million, and $44.3 million for research and development expenses in 2015, 2014 and 2013, respectively.

Corporate Development

We plan to develop, acquire, in-license or co-promote other products that address rare diseases. We are focused broadly on rare disease therapeutics and prioritizing those areas that best align with our core competencies and current therapeutic focus in the fields of pulmonology and infectious disease.

Manufacturing

ARIKAYCE is manufactured by Ajinimoto Althea, Inc., a Delaware corporation (Althea), in the US at a 50 liter scale. In September 2015, we entered into a commercial fill/finish services agreement with Althea to produce ARIKAYCE. Althea has the right to terminate this agreement upon written notice for our uncured material breach, if we are the subject of specified bankruptcy or liquidation events, or without cause with 24 months' prior written notice. In February 2014, we entered into a contract manufacturing agreement with Therapure Biopharma Inc., a Canadian corporation (Therapure) for the manufacture of ARIKAYCE at a 200 liter scale which we believe will be necessary to support commercialization. We have also identified certain second source suppliers for our supply chain, and plan to implement supply and quality agreements in preparation for commercialization of ARIKAYCE. In July 2014, we entered into a commercialization agreement with PARI Pharma GmbH (PARI), the manufacturer of our drug delivery nebulizer, to address our commercial supply needs. We currently produce INS1009, our investigational nebulized treprostinil prodrug, and plan to utilize third parties to manufacture INS1009 at a larger scale and the drug delivery device.

Intellectual Property

ARIKAYCE Patents and Trade Secrets

We own or license rights to more than 200 issued patents and pending patent applications in the US and in foreign countries, including more than 120 issued patents and pending patent applications related to ARIKAYCE. Our success depends in part on our ability to maintain proprietary protection surrounding our product candidates, technology and know-how; to operate without infringing the proprietary rights of others; and to prevent others from infringing our proprietary rights. We actively seek patent protection by filing patent applications, including on inventions that are important to the development of our business in the US, Europe, Canada, and selected other foreign markets that we consider key for our product candidates. These international markets generally include Australia, Japan, China, India, Israel, and Mexico.

Our patent strategy includes obtaining patent protection, where possible, on compositions of matter, methods of manufacture, methods of use, methods of treatment, dosing and administration regimens and formulations. We also rely on trade secrets, know-how, continuing technological innovation, in-licensing and partnership opportunities to develop and maintain our proprietary position.

We monitor for activities that may infringe our proprietary rights, as well as the progression of third-party patent applications that may have the potential to create blocks to our products or otherwise interfere with the development of our business. We are aware, for example, of US patents, and corresponding international counterparts, owned by third parties that contain claims related to treating lung infections using inhaled antibiotics. If any of these patents were to be asserted against us, we do not believe that our proposed products would be found to infringe any valid claim of these patents.

Reflecting our commitment to safeguarding proprietary information, we require our employees, consultants, advisors, collaborators and other third-party partners to sign confidentiality agreements to protect the exchange of proprietary materials and information. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

We own six US patents that cover the ARIKAYCE composition and its use in treating NTM. Upon ARIKAYCE approval for the treatment of NTM, these patents may be eligible for listing in the FDA Orange Book. These patents and their expiration dates (not taking into account any potential patent term extension) are as follows:

- US Patent No. 7,718,189 (expires June 6, 2025)
- US Patent No. 8,226,975 (expires August 15, 2028)
- US Patent No. 8,632,804 (expires December 5, 2026)
- US Patent No. 8,802,137 (expires April 8, 2024)
- US Patent No. 8,679,532 (expires December 5, 2026)
- US Patent No. 8,642,075 (expires December 5, 2026)

In addition, we own four pending US patent applications that cover the ARIKAYCE composition and its use in treating NTM. Upon ARIKAYCE approval for the treatment of NTM, these patents would be listed in the FDA Orange Book. We also own a pending US application that covers methods for making ARIKAYCE.

Three patents have been granted by the European Patent Office ("EPO") (European Patent Nos. 1581236, 1909759 and 2363114) that cover ARIKAYCE and its use in treating NTM. In addition, we have three applications pending before the EPO that cover ARIKAYCE and its use in treating NTM and one additional international application that will be filed in the EPO on or before November 15, 2016 that covers methods of treating NTM with ARIKAYCE. We also own a pending European application that covers methods of making ARIKAYCE. Thirty eight patents have also been issued in major foreign markets, e.g., Japan, China, Korea, Australia, and India, which cover ARIKAYCE and methods of using ARIKAYCE for treating NTM. Thirty seven foreign patent applications are pending that cover the ARIKAYCE composition and its use in treating NTM. We anticipate that in the US, we will have potential patent coverage for ARIKAYCE and its use in treating NTM, through at least February 2029, which includes a potential six months of pediatric exclusivity.

Through our agreements with PARI, we have license rights to US and foreign patents and applications that cover the eFlow Nebulizer System medical device. We have rights to use the nebulizers in clinical trials and we have entered into a commercial supply agreement with PARI.

The basic terms of utility patents issued in the US are the longer of 17 years from the issue date or 20 years from the earliest effective filing date, if the patent was in force on or was issued from a patent application that was filed prior to June 8, 1995; or 20 years from the earliest effective filing date, if the patent application was filed on or after June 8, 1995.

The basic term of foreign utility patents may vary in accordance with provisions of applicable local law, but is typically 20 years from the earliest effective filing date.

INS1009 Patents

We own US Patent No. 9,255,064 (expires October 24, 2034), which is the first patent to issue with claims covering INS1009. Other treprostinil prodrugs are also claimed and described in the patent. Methods of using treprostinil prodrugs, including INS1009, are described in the patent.

We own pending patent applications that if granted, would cover treprostinil analogs including INS1009, nanoparticle formulations of such treprostinil and prostacyclin analogs and methods for using such treprostinil analogs and nanoparticle formulations comprising the same in treating patients with pulmonary arterial hypertension and other diseases, as well as methods for manufacturing such prostacyclin analogs.

Trademarks

In addition to our patents and trade secrets, we have filed applications to register certain trademarks in the US and/or abroad, including INSMED, ARIKAYCE, and IPLEX. At present, we have received either registration or a notice of allowance for these marks from the US Patent and Trademark Office. We have also received foreign allowances or issued foreign registrations for certain of these marks. In October 2013, we learned that the EMA had no objection to our use of the name ARIKAYCE. In early 2014, we learned that the FDA conditionally approved our use of the name ARIKAYCE as our proposed trade name for our liposomal amikacin for inhalation product candidate. Our ability to obtain and maintain trademark registrations will in certain geographical locations depend on making use of the mark in commerce on or in connection with our products and approval of the trademarks for our products by regulatory authorities in each country.

License and Collaboration Agreements

ARIKAYCE-related License and Collaboration Agreements

Ajinomoto Althea, Inc.

In September 2015, we entered into a Commercial Fill/Finish Services Agreement (the "Fill/Finish Agreement") with Althea to produce, on a non-exclusive basis, ARIKAYCE in finished dosage form. Under the Fill/Finish Agreement, we are obligated to pay a minimum of $2.7 million for the batches of ARIKAYCE produced by Althea each calendar year during the term of the Fill/Finish Agreement. The Fill/Finish Agreement is effective as of January 1, 2015, has an initial term that ends on December 31, 2017 and may be extended for additional two year periods upon mutual written agreement of the Company and Althea at least one year prior to the expiration of its then-current term.

Either we or Althea may terminate the Fill/Finish Agreement upon the occurrence of certain events, including (i) material breach of the Fill/Finish Agreement by either party, provided such breach is not cured within 30 days after receipt by the breaching party of written notice of the breach or (ii) insolvency or bankruptcy of the other party. In addition, we may terminate the Fill/Finish Agreement without cause with 12 months' prior written notice to Althea, and Althea may terminate the Agreement without cause with 24 months' prior written notice.

PARI Pharma GmbH

We currently have a licensing agreement with PARI for use of the optimized eFlow Nebulizer System for delivery of ARIKAYCE in treating patients with NTM infections, CF and bronchiectasis. Under the licensing agreement, we have rights under several US and foreign issued patents, and patent applications involving improvements to the optimized eFlow Nebulizer System, to exploit such system with ARIKAYCE for the treatment of such indications, but we cannot manufacture such nebulizers except as permitted under our Commercialization Agreement with PARI (as discussed below). We currently have rights to use the nebulizers in clinical trials and also entered into a commercial supply agreement with PARI. Outside the EU, the eFlow Nebulizer System is labeled as investigational for use in our clinical trials in the US, Canada, Australia and Japan.

We have certain obligations under this licensing agreement in relation to specified licensed indications. With respect to CF, we are obligated to use commercially reasonable efforts to develop, obtain regulatory and reimbursement approval, market and sell ARIKAYCE in two or more major European countries. With respect to NTM, CF and bronchiectasis, we have specific obligations to use commercially reasonable efforts to achieve certain developmental and regulatory milestones by set deadlines. Additionally, for NTM, we are obligated to use commercially reasonable efforts to achieve certain commercial milestones in the US, Europe and Canada. The consequences of our failing to use commercially reasonable efforts to achieve these milestones are context-specific, but include ending PARI's non-compete obligation, making the license non-exclusive and terminating the license, in each case with respect to the applicable indication. Under the licensing agreement, we paid PARI an upfront license fee and PARI is entitled to receive milestone payments up to an aggregate of €4.3 million either in cash, qualified stock or a combination of both, at PARI's discretion, based on achievement of certain future milestone events including first acceptance of MAA submission (or equivalent) in the US of ARIKAYCE and the device, first receipt of marketing approval in the US for ARIKAYCE and the device, and first receipt of marketing approval in a major EU country for ARIKAYCE and the device. In addition, PARI is entitled to receive royalty payments in the mid-single digits on the net commercial sales of ARIKAYCE pursuant to the licensing agreement, subject to certain specified annual minimum royalties.

This license agreement will remain in effect on a country-by-country basis until the final royalty payments have been made with respect to the last country in which ARIKAYCE is sold, or until the agreement is otherwise terminated by either party. We have the right to terminate this license agreement upon written notice for PARI's uncured material breach, if PARI is the subject of specified bankruptcy or liquidation events, or if PARI fails to reach certain specified milestones. PARI has the right to terminate this license agreement upon written notice for our uncured material breach, if we are the subject of specified bankruptcy or liquidation events, if we assign or otherwise transfer the agreement to a third party that does not agree to assume all of our rights and obligations set forth in the agreement, or if we fail to reach certain specified milestones.

In July 2014, we entered into a Commercialization Agreement (the "PARI Agreement") with PARI for the manufacture and supply of eFlow nebulizer systems and related accessories (the "Device") as optimized for use with our proprietary liposomal amikacin for inhalation. The PARI Agreement envisages that PARI will undertake the manufacturing of the Device except in the case of certain defined supply failures, when we will have the right to make the Device and have it made by third parties (but not certain third parties deemed under the PARI Agreement to compete with PARI). The PARI Agreement has an initial term of fifteen years from the first commercial sale of ARIKAYCE pursuant to the licensing agreement (the "Initial Term"). The term of the PARI Agreement may be extended by us for an additional five years by providing written notice to PARI at least one year prior to the expiration of the Initial Term.

Therapure Biopharma Inc.

In February 2014, we entered into a Contract Manufacturing Agreement with Therapure for the manufacture of ARIKAYCE. Pursuant to the Agreement, we collaborated with Therapure to construct a production area for the manufacture of ARIKAYCE in Therapure's existing manufacturing facility in Mississauga, Ontario, Canada. Therapure manufactures ARIKAYCE for us on a non-exclusive basis. The agreement has an initial term of five years from the first date on which Therapure delivers ARIKAYCE to us after we obtain permits related to the manufacture of ARIKAYCE, and will renew automatically for successive periods of two years each, unless terminated by either party by providing the required two years' prior written notice to the other party. Notwithstanding the foregoing, the parties have rights and obligations under the agreement prior to the commencement of the initial term. Under the agreement, we are obligated to pay certain minimum amounts for the batches of ARIKAYCE produced each calendar year. The agreement allows for termination by either party upon the occurrence of certain events, including (i) the material breach by the other party of any provision of the agreement or the quality agreement expected to be entered into between the parties, or (ii) the default or bankruptcy of the other party. In addition, we may terminate the agreement for any reason upon no fewer than one hundred eighty days' advance notice. Costs incurred under this agreement are being recorded as a component of research and development expense until such time as we receive US FDA approval for ARIKAYCE.

SynteractHCR, Inc.

On December 30, 2014, we entered into Work Order 1, pursuant to a Master Agreement for Services with SynteractHCR, Inc., ("Synteract") dated as of August 27, 2014, as amended on December 23, 2014, pursuant to which we retained Synteract to perform implementation and management services in connection with certain clinical trials pursuant to a specific protocol of pharmaceutical products under development by us or under our control. Synteract is providing comprehensive services for the 212 study. Prior to the execution of the Work Order, Synteract was providing such services pursuant to a Letter of Intent, dated August 25, 2014. Based on work orders signed to date for the 212 study, we anticipate that aggregate costs relating to the Synteract work orders will be approximately $40 million over the period of the study. In addition, we signed work orders with Synteract related to the follow-on 312 study. Based on work orders signed to date for the 312 study, we anticipate that aggregate costs relating to the Synteract work orders will be approximately $20 million over the period of the study.

Cystic Fibrosis Foundation Therapeutics, Inc.

In 2004 and 2009, we entered into research funding agreements with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) whereby we received $1.7 million and $2.2 million for each respective agreement in research funding for the development of ARIKAYCE. If ARIKAYCE becomes an approved product for CF in the US, we will owe a payment to CFFT of up to $13.4 million that is payable over a three-year period after approval as a commercialized drug in the US. Furthermore, if certain global sales milestones are met within 5 years of the drug commercialization, we would owe an additional payment of $3.9 million. Under the 2009 agreement, in the event we terminate development of ARIKAYCE prior to first commercial sale of a product containing ARIKAYCE for a period of 360 continuous days, and such termination is not for reasons outside of our reasonable control, then at CFFT's election and within 180 days of such termination, CFFT (1) may elect to develop ARIKAYCE and (2) will have the right to receive from us an exclusive (subject to certain exceptions), royalty-free, sub-licensable license to use, develop, sell and commercialize a product containing ARIKAYCE in the treatment of certain infections in CF patients or pulmonary disease.

INS1009-related License and Other Collaboration Agreements

Device Supply and Clinical Investigation Agreement Relating to INS1009

Respironics —In November 2015, we entered into an agreement with Respironics Inc., a division of Philips (Respironics), for the clinical supply of devices to be used in the development of INS1009 for PAH. The agreement calls for payments to Respironics upon the achievement of certain clinical milestones relating to the development of INS1009 aggregating $7.6 million. In addition, we will be required to pay a royalty on net sales of the product, if any.

License Agreements and Other Collaboration Agreements

Ipsen and Genentech —Prior to 2007, we focused on development and commercialization of IPLEX for the treatment of growth failure in children with severe primary IGF-deficiency. IPLEX was approved by the FDA for treatment of severe primary IGF-1 deficiency in December 2005 and was commercially launched in the second quarter of 2006. We subsequently withdrew IPLEX from the market in connection with a patent infringement settlement agreement among us, Ipsen (formerly Tercica), and Genentech. In connection with the settlement, we were granted a license or sublicense as applicable to patents held by Ipsen and Genentech to develop IPLEX in certain medical indications in the US and foreign territories, subject to certain opt-in and other rights retained by Ipsen and Genentech. In November 2008 we gained Royalty-Free Worldwide Rights for IPLEX from Ipsen and Genentech in connection with potential expanded access ALS programs.

Eleison —In February 2011, we entered into an agreement with Eleison Pharmaceuticals whereby we granted Eleison an exclusive license for Inhaled CISPLATIN Lipid Complex. The license gives Eleison the right to develop, manufacture and commercialize inhaled CISPLATIN Lipid Complex for cancers affecting the lung. Payments totaling $1.0 million were received in 2011 and were recorded in license fees.

Premacure (now Shire plc) —In May 2012, we entered into an agreement with Premacure pursuant to which we granted to Premacure an exclusive, worldwide license to develop manufacture and commercialize IGF-1, with its natural binding protein, IGFBP-3, for the prevention and treatment of complications of preterm birth (the "Premacure License Agreement"). In March 2013, we amended the Premacure License Agreement to provide Premacure with the option to pay us $11.5 million and assume any of our royalty obligations to other parties in exchange for a fully paid license. In March 2013, Shire plc announced that they acquired Premacure. In April 2013 Shire exercised this option and paid us $11.5 million, and as a result we are not entitled to future royalties from Shire.

Competition

The biotechnology and pharmaceutical industries are highly competitive. We face potential competitors from many different areas including commercial pharmaceutical, biotech and device companies, academic institutions and scientists, other smaller or earlier stage companies and non-profit organizations developing anti-infective drugs and drugs for respiratory diseases. Many of these companies have greater human and financial resources and may have product candidates in more advanced stages of development and may reach the market before our product candidates. Competitors may develop products that are more effective, safer or less expensive or that have better tolerability or convenience. We also may face generic competitors where third-party payers will encourage use of the generic products. Although we believe that our formulation delivery technology, respiratory and anti-infective expertise, experience and knowledge in our specific areas of focus provide us with competitive advantages, these potential competitors could reduce our commercial opportunity.

NTM competitive overview

Our major competitors include pharmaceutical and biotechnology companies that have approved therapies or therapies in development for the treatment of chronic lung infections. While some companies have expressed interest in studying their products for NTM, we are not aware of any companies that are currently conducting clinical trials for the treatment of NTM lung disease. There are no approved inhaled therapies specifically indicated for NTM lung infections in North America, Europe or Japan but there is an ATS/IDSA-recommended treatment regimen that is utilized.

Government Regulation

Orphan Drugs

European Union

The European Commission grants orphan drug designation to promote the development of drugs or biologics (1) for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the EU, or (2) for life threatening, seriously debilitating or serious and chronic condition in the EU where, without incentives, sales of the drug in the European Economic Area (the European Union plus, Iceland, Lichtenstein, and Norway) (EEA) are unlikely to be sufficient to justify its development. Orphan drug designation is available either if no other satisfactory method of diagnosing, preventing or treating the condition is approved in the EEA or if such a method does exist but the proposed orphan drug will be of significant benefit to patients.

If a drug with an orphan drug designation subsequently receives a marketing authorization for a therapeutic indication which is covered by such designation, the drug is entitled to orphan exclusivity. Orphan exclusivity means that the EMA or national Medicines Agency may not accept another application for authorization, or grant an authorization, for a same or similar drug for the same therapeutic indication. Competitors may receive such a marketing authorization despite orphan exclusivity, provided that they demonstrate that the existing orphan product is not supplied in sufficient quantities or that the 'second' drug or biologic is clinically superior to the existing orphan product. The 'second' drug may but need not to have an orphan designation as well. The period of orphan exclusivity is ten years, which can be extended by two years where an agreed pediatric investigation plan has been implemented (see Pediatric Information section below). The exclusivity period may also be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Each orphan designation carries the potential for one market exclusivity for all the therapeutic indications that are covered by the designation. A product that has several separate orphan designations has several separate market exclusivities.

Orphan drug designation also provides opportunities for free protocol assistance and fee reductions for access to the centralized regulatory procedure or fee exemptions for companies with a small and medium enterprises (SMEs) status. In addition, Member States may provide national benefits to orphan drugs, such as early access to the reimbursement procedure or exemption from the turnover tax imposed on pharmaceutical companies.

The orphan designation may be applied for at any time during the development of the drug but before the application for marketing authorization. At the time of marketing authorization, the criteria for orphan designation are examined again, and the Commission decides on the maintenance of the orphan designation. The non-maintenance of the orphan designation means that the drug loses its orphan status and thus no longer benefit from orphan exclusivity, fee reductions or exemptions, and national benefits.

United States

Under the Orphan Drug Act (ODA), the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition ("rare" is generally defined as a disease or condition for which the drug intended affects fewer than 200,000 people in the US) if it meets certain criteria specified in the ODA and FDA's implementing regulations at 21 CFR Part 316. After the FDA grants orphan drug designation, the drug and the specific intended use(s) for which it has obtained designation are listed by FDA in a publicly-accessible database.

Orphan drug designation qualifies the drug sponsor for various development incentives of the ODA, including tax credits for qualified clinical testing, and a waiver of the NDA application user fee (unless the application seeks approval for an indication not included in the orphan drug designation). Orphan drug designation also affords the company a period of marketing exclusivity upon approval of the drug. Specifically, the first NDA applicant with an FDA orphan drug designation for a particular active moiety to receive FDA approval of the drug for an indication covered by the orphan designation is entitled to a seven-year exclusive marketing period, often referred to as orphan drug exclusivity, in the US for that drug and indication. During the orphan drug exclusivity period, the FDA may not approve any other applications to market the same drug for the same indication for use, except in limited circumstances, such as a showing of clinical superiority to the product that has orphan drug exclusivity. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition.

However, orphan drug designation does not alter the timing or scope of the regulatory review and approval process; the sponsor must still submit evidence from clinical and non-clinical studies sufficient to demonstrate the safety and effectiveness of the drug.

Drug Approval

European Union

Marketing Authorization Application

To obtain approval of a drug under the EU regulatory system, an application for a marketing authorization may be submitted under a centralized, a decentralized or a national procedure. The centralized procedure, which is compulsory for medicines produced by certain biotechnological processes or for orphan drugs, provides for the grant of a single marketing authorization that is valid for all EU member states, which grants the same rights and obligations in each member states as a national marketing authorization. As a general rule, only one marketing authorization may be granted for drugs approved through the centralized procedure. Pursuant to the European Economic Agreement between the European Union and the EFTA countries, the marketing authorization is also relevant for the three EFTA countries (Iceland, Lichtenstein, Norway).

Under the centralized procedure, the Committee for Human Medicinal Products for Human Use (CHMP), the EMA's main scientific committee, is required to adopt an opinion on a valid application within 210 days, excluding clock stops when additional information is to be provided by the applicant in response to questions. More specifically, on day 120 of the procedure, once the CHMP has received the preliminary assessment reports and opinions from the Rapporteur and Co-Rapporteur designated by the CHMP, it adopts a list of questions, which are sent to the applicant together with the CHMP's overall conclusions. Applicants then have three months to respond to the CHMP (and can request a three-month extension). The Rapporteur and Co-Rapporteur assess the applicant's replies, revise the assessment report as necessary and may prepare a list of outstanding issues. The revised assessment report and list of outstanding issues are sent to the applicant together with the CHMP's recommendation by day 180 of the procedure. Applicants then have one month to respond to the

CHMP (and can request a one or two-month extension). The Rapporteur and Co-Rapporteur assess the applicant's replies, submit them for discussion to the CHMP and prepare a final assessment report. Once its scientific evaluation is completed, the CHMP gives a favorable or unfavorable opinion as to whether to grant the marketing authorization. After the adoption of the CHMP opinion, a decision must be adopted by the European Commission, after consulting the Standing Committee of the Member States. The European Commission prepares a draft decision and circulates it to the member states; if the draft decision differs from the CHMP opinion, the Commission must provide detailed explanations. The European Commission adopts a decision within 15 days of the end of the consultation procedure.

Accelerated Procedure, Conditional Approval and Approval Under Exceptional Circumstances

Various programs, including accelerated procedure, conditional approval and approval under exceptional circumstances, are intended to expedite or simplify the approval of drugs that meet certain qualifications. The purpose of these programs is to provide important new drugs to patients earlier than under standard approval procedures.

For drugs which are of major interest from the point of view of public health, in particular from the viewpoint of therapeutic innovation, applicants may submit a substantiated request for accelerated assessment. If the CHMP accepts the request, the review time is reduced from 210 to 150 days.

Furthermore, for certain categories of medicinal products, marketing authorizations may be granted on the basis of less complete data than is normally required in order to meet unmet medical needs of patients or in the interest of public health. In such cases, the company may request, or the CHMP may recommend, the granting of a marketing authorization, subject to certain specific obligations; such marketing authorization may be conditional or under exceptional circumstances. The timelines for the centralized procedure described above also apply with respect to applications for a conditional marketing authorization or marketing authorization under exceptional circumstances.

Conditional marketing authorizations may be granted for products designated as orphan medicinal products, if all of the following conditions are met: (1) the risk-benefit balance of the product is positive, (2) the applicant will likely be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs, and (4) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required.

Conditional marketing authorizations are valid for one year, on a renewable basis until the holder provides a comprehensive data package. The granting of conditional marketing authorization depends on the applicant's ability to fulfill the conditions imposed within the agreed upon deadline. They are subject to "conditions", i.e. the holder is required to complete ongoing studies or to conduct new studies with a view to confirming that the benefit-risk balance is positive or to fulfill specific obligations in relation to pharmacovigilance. Once the holder has provided a comprehensive data package, the conditional marketing authorization is replaced by a 'regular' marketing authorization.

Marketing authorizations under exceptional circumstances may be granted where the applicant demonstrates that, for objective and verifiable reasons, he is unable to provide comprehensive data on the efficacy and safety of the drug under normal conditions of use. Such marketing authorizations are subject to certain conditions, in particular relating to safety of the drug, notification of incidents relating to its use or actions to be taken. They are valid for an indefinite period of time, but the conditions upon which they are based are subject to an annual reassessment in order to ensure that the risk-benefit balance remains positive.

Exclusivities

If an approved drug contains a new active substance, it is protected by data exclusivity for eight years as from the notification of the Commission decision granting the marketing authorization and then by marketing protection for two or three years. Overall, the drug is protected for ten or eleven years against generic competition, and no additional exclusivity protection is granted for any new development of the active substance it contains.

During the eight-year period of data exclusivity, competitors may not refer to the marketing authorization dossier of the approved drug for regulatory purposes. During the period of marketing protection, competitors may not market their competitor drugs. The period of marketing protection is normally two years but may become three years if, during the eight-year data exclusivity period, a new therapeutic indication is approved that is considered as bringing a significant clinical benefit over existing therapies.

Medical Devices Regulations

In the EU, the marketing of medical devices is not subject to a prior approval by a health authority, but, depending on the class of device, may require prior review by a Notified Body. Notified Bodies are technical review bodies that are accredited and supervised by national health authorities. They conduct conformity assessment procedures of, among others, medical devices.

Medical devices are generally governed by Directive 93/42/EEC on Medical Devices that harmonizes the conditions for placing medical devices on the European market. This Directive however does not regulate certain important marketing aspects, such as advertising or pricing and reimbursement, which remain governed by national law.

Directive 93/42 requires medical devices to meet the essential requirements which are enumerated in the annexes to the Directive. Compliance with those requirements is demonstrated by the CE mark as the manufacturer may only affix the CE mark if he may declare conformity with the essential requirement for each medical device that is marketed. Directive 93/42 provides recourse to harmonized European standards in order to facilitate compliance with the essential requirements. Harmonized standards provide a presumption of conformity with the essential requirements.

Directive 93/42 institutes several conformity assessment procedure. The relevant conformity assessment procedure depends on the type of medical device and the risks involved. Devices are divided in four groups: Class I, Class IIa, Class IIb, and Class III. Class I devices present the lowest level of risk so that, for most of these devices the manufacturer can self-certify the product and need not rely on certification by a Notified Body. For the other classes, a Notified Body must review the manufacturer's procedures and/or the product. Every device is initially classified by the manufacturer. However, the Notified Body may dispute the classification and assert that the device should be included in a class requiring stricter conformity assessment procedures. Specific rules apply to custom-made medical devices, medical devices that are used in clinical trials, and medical devices that incorporate a medicinal ingredient.

For classes of devices other than Class I, a manufacturer must have a Notified Body test and certify conformity of its design and production procedures or its products with the essential requirements of Directive 93/42. Certification takes the form of a certificate of conformity issued by the Notified Body, which is valid throughout the European Union. Upon certification by the Notified Body, the manufacturer affixes the CE mark to the medical device, which allows the product to move freely within the European Union and thus prevents EU Member States from restricting sales and marketing

of the devices, unless such measure is justified on the basis of evidence of non-compliance. Ultimately, the manufacturer is responsible for the conformity of the device with the essential requirements and for the affixing of the CE mark.

Manufacturers of medical devices are subject to materiovigilance obligations that require reporting of incidents or near incidents related to the use of a medical device, which incidents may demonstrate the need for corrective action by the manufacturer. In addition, Notified Bodies regularly re-assess the conformity of a medical device to the essential requirements of Directive 93/42 and may from time to time audit the manufacturer and may, where needed, suspend or withdraw the manufacturer's certificate of conformity.

United States

In the United States, pharmaceutical products are subject to extensive regulation by the FDA and other government bodies. The Federal Food, Drug, and Cosmetic Act (FDCA) and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable US requirements at any time during product development, approval, or after approval may subject a company to a variety of administrative or judicial sanctions, such as imposition of clinical holds, FDA refusal to accept for filing or approve new drug applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, civil penalties, and criminal prosecution.

Pharmaceutical product development in the US may include:

- 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 investigational new drug application, or IND, which must become effective before clinical trials may begin;
- Approval of the protocol by an independent institutional review board, or IRB before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug for each indication;
- Submission to the FDA of a NDA;
- Satisfactory completion of an FDA advisory committee review, if applicable;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

The sponsor must submit adequate tests by all methods reasonably applicable to show that the drug is safe for use under the conditions prescribed, recommended or suggested in the proposed labeling. The sponsor must submit substantial evidence, generally consisting of adequate and well-controlled clinical investigations, to establish that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling. In certain cases, FDA may determine that a drug is effective based on one clinical study plus confirmatory evidence. Satisfaction of FDA pre-market approval requirements typically takes

many years and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, formulation and toxicity, pharmacology, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements including FDA's good laboratory practices regulations and USDA's regulations implementing the Animal Welfare Act. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature, and a proposed clinical trial protocol, among other things, to the FDA as part of an IND application. Certain non-clinical tests, such as animal tests of reproductive toxicity and carcinogenicity, 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 clinical 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 (healthy volunteers or patients) under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with all applicable federal regulations and guidance, including those pertaining to good clinical practice, or GCP, standards that are meant to protect the rights, safety, and welfare of human subjects and to define the roles of clinical trial sponsors, investigators, and monitors; as well as (ii) 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. Each protocol involving testing of a new drug in the US (whether in patients or healthy volunteers) must be included in the IND submission, and FDA must be notified of subsequent protocol amendments. In addition, the protocol must be reviewed and approved by an IRB, and all study subjects must provide informed consent. Typically each institution participating in the clinical trial will require review of the protocol before any clinical trial before it commences at that institution. 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. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and there are additional, more frequent reporting requirements for suspected serious adverse events.

A study sponsor might choose to discontinue a clinical trial or a clinical development program for a variety of reasons. The FDA may impose a temporary or permanent clinical hold, or other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial subjects. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential pre-approval phases, but the phases may overlap or be combined. In Phase 1, short term (typically less than a few months) testing is conducted in a small group of subjects (typically 20-100), who may be patients with the target disease or condition or healthy volunteers, to evaluate its safety, determine a safe dosage range, and identify side effects. In Phase 2, the drug is given to a larger group (up to several hundred) of subjects with the target condition to further evaluate its safety and gather

preliminary evidence of efficacy. Phase 3 studies typically last between several months and two years. In Phase 3, the drug is given to a large group of subjects with the target disease or condition (several hundred to several thousand), often at multiple geographical sites, to confirm its effectiveness, monitor side effects, and collect data to support drug approval. In some cases, FDA may require post-market studies, known as Phase 4 studies, to be conducted as a condition of approval in order to gather additional information on the drug's effect in various populations and any side effects associated with long-term use. Depending on the risks posed by the drugs, other post-market requirements may be imposed. Only a small percentage of investigational drugs complete all three phases and obtain marketing approval.

NDA Application

After completion of the required clinical testing, an NDA can be prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the US. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, and annual product and establishment user fees also apply. These fees are typically increased annually.

The FDA has 60 days from its receipt of a NDA to determine whether the application will be accepted for filing based on the FDA's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins a substantive review. Under the statute and implementing regulations, FDA has 180 days (the "initial review cycle") from the date of filing to issue either an approval letter or a complete response letter, unless the review period is adjusted by mutual agreement between FDA and the applicant or as a result of the applicant submitting a major amendment. In practice, the performance goals established pursuant to the Prescription Drug User Fee Act have effectively extended the initial review cycle beyond 180 days. FDA's current performance goals call for FDA to complete review of 90 percent of standard (non-priority) NDAs within 10 months of receipt and within six months for priority NDAs, but two additional months are added to standard and priority NDAs for an NME.

The FDA may refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes outside clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving a NDA, the FDA will typically inspect one or more clinical sites to assure compliance with Good Clinical Practice. Additionally, the FDA will typically inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance with current good manufacturing practices is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication or indications studied. FDA also reviews the proposed labeling submitted with the NDA and typically requires changes in the labeling text.

After the FDA evaluates the NDA and the manufacturing and testing facilities, it issues either an approval letter or a complete response letter. Complete response letters generally outline the deficiencies in the submission and delineate the additional testing or information needed in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has

committed to reviewing 90 percent of resubmissions within two or six months from receipt depending on the type of information included.

An approval letter authorizes commercial marketing of the drug for the approved indication or indications and the other conditions of use set out in the approved prescribing information. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

As a condition of NDA approval, the FDA may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy and may impose other conditions, including labeling restrictions that can materially affect the potential market and profitability of the drug. As a condition of approval, or after approval, the FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, to mitigate any identified or suspected serious risks. The REMS may 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.

Expedited Review and Approval of Eligible Drugs

The FDA's 21 CFR 314 Subpart H (Accelerated Approval) regulations allow certain drugs, for serious or life-threatening conditions, to be approved on the basis of surrogate endpoints (i.e., clinical endpoints other than survival or irreversible morbidity), which can substantially reduce time to approval. As a condition of approval under Subpart H, the FDA may require certain adequate and well-controlled post-marketing clinical studies to verify and describe clinical benefit of the product, and may impose restrictions on distribution to assure safe use. Post marketing studies would usually be required to be studies already underway at the time of the accelerated approval. In addition, all promotional materials for an accelerated approval drug must be submitted to FDA prior to use. If the required post-marketing studies fail to verify the clinical benefit of the drug, or if the applicant fails to perform the required post-marketing studies with due diligence, the FDA may withdraw approval of the drug following a hearing conducted in accordance with the agency's regulations. Under Subpart H, the agency may also withdraw approval of a drug if, among other things, the promotional materials for the product are false or misleading, or other evidence demonstrates that the drug product is not shown to be safe or effective under its conditions of use.

The FDA also has various programs—fast track designation, priority review, and breakthrough designation—that are intended to expedite or streamline the process for the development and FDA review of drugs that meet certain qualifications. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures. The programs each have different eligibility criteria and provide different benefits, and can be applied either alone or in combination depending on an applicant's circumstances. Fast track designation applies to a drug that is intended to treat a serious condition and for which nonclinical or clinical data demonstrate the potential to address unmet medical need. It should be requested at the time of IND submission or ideally no later than the pre-NDA meeting. FDA must respond to requests for fast track designation within 60 days of receipt of the request. If granted, the manufacturer is eligible for actions to expedite development and review, such as frequent interaction with the review team, as well as for rolling review, meaning that the applicant may submit sections of the application as they are available. The timing of FDA's review of these sections depends on a number of factors, and the review clock does not start running until the agency has received a complete NDA submission. FDA may withdraw fast track designation if the agency determines that the designation is no longer supported by data emerging in the clinical trial process.

Priority review applies to an application (both original and efficacy supplement) for a drug that treats a serious condition and that, if approved, would provide a significant improvement in safety or effectiveness. It also applies to any supplement that proposes a labeling change pursuant to a report on a pediatric study. A request for priority review is submitted at the time of NDA or supplemental NDA submission. FDA must respond within 60 days of receipt of the request. If granted, the review time is shortened from the standard 10 months to 6 months, with two additional months in the case of an NME.

Breakthrough therapy designation was created under the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA). Breakthrough therapy designation applies to a drug that is intended to treat a serious condition and for which preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies. It can be requested with the IND submission and ideally no later than the end-of-phase 2 meeting. FDA must respond within 60 days of receipt of the request. If granted, the applicant receives intensive guidance on efficient drug development, intensive involvement of senior managers and experienced review and regulatory health project management staff in a proactive, collaborative, cross-disciplinary review, rolling review, and other actions to expedite review. Designation may be rescinded if the product no longer meets the criteria for breakthrough therapy designation.

The 2012 Generating Antibiotic Incentives Now (GAIN) Act created new incentives for the development of new therapies for serious and life-threatening infections. Drugs that are designated as Qualified Infectious Disease Products, or QIDPs, are eligible for priority review and fast track designation, and well as market exclusivity. A product is eligible if it is an antibacterial or anti-fungal drug for human use that is intended to treat serious or life-threatening infections, including: those caused by an anti-bacterial or anti-fungal resistant pathogen, including novel or emerging infectious pathogens; or caused by qualifying pathogens listed by the FDA. A drug sponsor may request that FDA designate its product as a QIDP at any time prior to NDA submission. FDA must make a QIDP determination within 60 days of receiving the designation request.

Exclusivities

After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension on a single patent. The allowable patent term extension is calculated as half of the drug's testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval) up to a maximum of five years. The time can be shortened if FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years. For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which a NDA has not been submitted.

A variety of non-patent exclusivity periods are available under the FDCA that can delay the submission or approval of certain applications for competing products.

A five-year period of non-patent exclusivity within the United States is granted to the first applicant to gain approval of a NDA for a new chemical entity (NCE). An NCE is a drug that contains no active moiety (the molecule or ion responsible for the action of the drug substance) that has been approved by FDA in any other application submitted under section 505(b) of the Act. During the

exclusivity period for a new chemical entity, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company that references (i.e., relies on FDA prior approval of) the NCE drug. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement with respect to a patent listed with the FDA for the reference NDA.

A three year period of non-patent exclusivity is granted for a drug product that contains an active moiety that has been previously approved, when the application contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to approval of the application, for example, for new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations, which means that FDA may approve applications for other versions of the original, unmodified drug product. Where this form of exclusivity applies, it prevents FDA approval of an ANDA or 505(b)(2) NDA subject to the exclusivity for the three-year period; however, FDA may accept and review ANDAs or 505(b)(2) NDAs during the three year period.

Five year and three year exclusivities also do not preclude FDA approval of a 505(b)(1) application for a duplicate version of the drug during the period of exclusivity, provided that the 505(b)(1) conducts or obtains a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Products with QIDP designation may receive a five year extension of other non-patent exclusivities for which the drug is also eligible. This exclusivity applies only with respect to drugs that are first approved on or after July 9, 2012. The exclusivity does not prevent FDA from approving a subsequent application for a change to the QIDP-designated drug that results in a new indication, route of administration, dosing, schedule, dosage form, delivery system, delivery device, or strength. For example, an approved product with orphan designation and QIDP designation would have twelve years of marketing exclusivity.

Medical Device Regulation

Medical devices may receive marketing authorization from FDA as stand-alone devices, or in some cases, may receive marketing authorization as part of a combination product. In either case, the ultimate product will need to satisfy FDA requirements. The primary pathways for marketing authorization for devices in the United States are 510(k) clearance or premarket approval (PMA).

Medical devices are also subject to certain post-clearance, post-approval requirements. Those requirements include continuing Quality System Regulation compliance, Medical Device Reporting, Correction and Removal, and requirements governing labeling and promotional advertising.

The FDCA provides for the exemption of medical devices intended for investigational use from certain regulatory requirements if such devices comply with prescribed procedures and conditions. For example, devices intended for investigational use may be exempted from premarket notification and premarket approval requirements. Investigational devices must bear a label that states the following: "CAUTION—Investigational device. Limited by Federal (or US) law to investigational use." The labeling may not represent that the device is safe or effective for the purposes for which it is being investigated.

Combination Products

A combination product is a product comprising two or more regulated components (e.g., a drug and device) that are combined into a single product, co-packaged, or sold separately but intended for co-administration, as evidenced by the labeling for the products. A drug that is administered using an inhaler is an example of a combination drug/device product.

FDA is divided into various Centers, which each have authority over a specific type of product. NDAs are reviewed by personnel within the Center for Drug Evaluation and Research, while device applications and premarket notifications are reviewed by the Center for Devices and Radiological Health. When reviewing a drug/device combination product, FDA must assign a lead Center to review the product, based on the combination product's primary mode of action, or PMOA, which is the single mode of a combination product that provides the most important therapeutic action of the combination product. The Center that regulates that portion of the product that generates the PMOA becomes the lead evaluator. If there are two independent modes of action, neither of which is subordinate to the other, the FDA makes a determination as to which Center to assign the product based on consistency with other combination products raising similar types of safety and effectiveness questions or to the Center with the most expertise in evaluating the most significant safety and effectiveness questions raised by the combination product.

When evaluating an application, a lead Center may consult other Centers and apply the standards that would be applicable but still retain complete reviewing authority, or it may collaborate with another Center, by which the Center assigns review of a specific section of the application to another Center, delegating its review authority for that section. Typically, the FDA requires a single marketing application submitted to the Center selected to be the lead evaluator, although the agency has the discretion to require separate applications to more than one Center. One reason to submit multiple applications is if the applicant wishes to receive some benefit that accrues only from approval under a particular type of application, like new drug product exclusivity. If multiple applications are submitted, each may be evaluated by a different lead Center.

Like their constituent products—e.g., drugs and devices—combination products are highly regulated and subject to a broad range of post marketing requirements including cGMPs, adverse event reporting, periodic reports, labeling and advertising and promotion requirements and restrictions.

Disclosure of Clinical Trial Information

Under US and certain foreign laws intended to improve clinical trial transparency, sponsors of clinical trials may be required to register and disclose certain information about their clinical trials. This can include information related to the investigational drug, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial. This information is then made publicly available. Sponsors also may be obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly-available information to gain knowledge regarding the progress of development programs.

Other US Post-approval Regulatory Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements, including those relating to advertising, promotion, adverse event reporting, recordkeeping, and good manufacturing practices, as well as registration, listing, and inspection. 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.

FDA regulates the content and format of prescription drug labeling, advertising, and promotion, including direct-to-consumer advertising and promotional Internet communications. FDA also establishes parameters for permissible non-promotional communications between industry and the medical community, including industry-supported scientific and educational activities. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion for uses not consistent with the approved labeling, and a company that is found to have improperly promoted off-label uses or otherwise not to have met applicable promotion rules may be subject to significant liability under both the FDCA and other statutes, including the False Claims Act.

Manufacturers are subject to requirements for adverse event reporting and submission of periodic reports following FDA approval of a NDA.

All aspects of pharmaceutical manufacture must conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA during which the FDA inspects manufacturing facilities to assess compliance with cGMPs. 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 areas of production and quality control to maintain compliance with cGMPs.

Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Changes to some of the conditions established in an approved application, including changes in indications, labeling, product formulation, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement, in some cases before the change may be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

The FDA also may require post market studies, known as phase 4 studies, and may require a REMS, which could restrict the distribution or use of the product.

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, or failure of phase 4 studies to meet their specified endpoints, may result in revisions to the approved labeling to add new safety information; or the need to conduct additional post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program; or recall of the product and withdrawal of the NDA.

Noncompliance with postmarket requirements can result in one or more of the following consequences:

- Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- Warning letters;
- 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.

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.

Pediatric Information

European Union

In the European Union, new drugs (i.e. drugs containing a new active substance) for adults, must also be tested in children. This mandatory pediatric testing is carried out through the implementation of a pediatric investigation plan, or PIP, which is proposed by the applicant and approved by the EMA. A PIP contains all the studies to be conducted and measures to be taken in order to support the approval of the new drug, including pediatric pharmaceutical forms, in all subsets of the pediatric population. Validation of the marketing authorization application for adults is subject to the implementation of the PIP, subject to one or more waivers or deferrals. On the one hand, the PIP may allow a deferral for one or more of the studies or measures included therein in order not to delay the approval of the drug in adults, and, on another hand, the EMA may grant either a product-specific waiver for the (adult) disease/condition or one or more pediatric subsets or a class waiver for the disease/condition. PIPs are subject to modifications from time to time, when they no longer are workable. Prior to obtaining the validation of a marketing authorization application for adults, the applicant has to demonstrate compliance with PIP at the time of submission of the application. In the case of orphan medicinal products, completion of an approved PIP can result in an extension of the market exclusivity period from ten to twelve years.

United States

Under the Pediatric Research Equity Act of 2003, or PREA, NDAs and NDA supplements 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 drug is safe and effective. The FDA may, on its own initiative or at the request of an applicant, grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted. Under the Best Pharmaceuticals for Children Act (BPCA), pediatric research is incentivized by the possibility of six additional months of pediatric exclusivity, which if granted, is added to existing exclusivity periods and patent terms listed for the applicable drug in the FDA's Orange Book at the time the sponsor satisfies FDA's "written request" for pediatric research. Sponsors may seek to negotiate the terms of a written request during drug development. While the sponsor of an orphan designated drug may not be required to perform pediatric studies under PREA, they are eligible to participate in the incentives under the BPCA.

Regulation Outside the US and Europe

In addition to regulations in the US and Europe, we will be subject to a variety of regulations in other jurisdictions governing clinical studies of our candidate products. Whether or not we obtain

FDA approval for a product, we must obtain approval of a product by the comparable regulatory authorities of countries outside the US before we can commence clinical studies or marketing of the product in those countries. The requirements for approval and the approval process vary from country to country, and the time may be longer or shorter than that required for FDA approval. Furthermore, we must obtain any required pricing approvals in addition to regulatory approval prior to launching the product in the approving country.

Health Canada

Health Canada (HC) is the government agency that provides regulatory and marketing approval for drugs and therapeutic products in Canada. The upcoming Legislative and Regulatory Modernization (LRM) is the most significant drug regulatory system reform in Canada in more than 50 years and is expected to overhaul Canada's Food and Drugs Act and Regulations. The LRM supports a 'lifecycle' regulatory approach and is focused on strengthening evidence-based decision making, good regulatory planning, licensing, post-licensing, accountability, authority and enforcement. Through this framework, HC intends to improve the market authorization process and implement necessary regulatory frameworks. In October 2010, HC accelerated its modernization efforts. This included the proposed regulatory pathways for Orphan Drugs (harmonized with US/EU regulations).

Japan

The Minister of Health, Labor and Welfare is the government agency that provides regulatory approval for pharmaceutical products in Japan. Parties engaged in manufacture or sale of products in Japan must receive the approval of the Minister of Health, Labor and Welfare. The Pharmaceutical Affairs Law of Japan requires a license for marketing authorization when importing to Japan and selling pharmaceutical products manufactured in other countries. It also requires a foreign manufacturer to get each of its manufacturing sites certified as a manufacturing site of pharmaceutical products to be marketed in Japan. To receive a license for marketing authorization, the manufacturer or seller must, at the very least, employ the certain manufacturing marketing, quality and safety personnel. A license for marketing authorization may not be granted if the quality management methods and post marketing safety management methods applied with respect to the pharmaceutical product fail to conform to the standards stipulated in the ordinances promulgated by the Ministry of Health, Labor and Welfare.

In addition to the licensing requirements for entities that engage in manufacturing, importing and sales of medical products as mentioned above, the law also requires that the medical products have obtained approval before they are marketed and sold in Japan. The process for the approval includes such elements as evaluation and testing of trustworthiness of the clinical trial, testing of quality, efficacy, absorption and egestion, toxicity, and safety of the products. The time required for the approval process varies depending on the product, but it can be years. The product also needs approval for pricing to be applied for redemption of health insurance. The medical products which once are approved and marketed are also subject to regular post-marketing vigilance of safety and quality under the standards of Good Manufacturing Practice.

Australia

The Therapeutic Goods Administration ("TGA") is the regulatory body, under the Australian Department of Health, responsible for conducting assessment and monitoring activities of therapeutic goods in Australia. Products under the jurisdiction of the TGA include prescription medicines, medical devices (simple and complex), diagnostic products, vaccines, and biologics. Activities of the TGA include classifying the product based on risk to the person, implementing appropriate regulatory

controls for the manufacturing processes, and monitoring approved products with a comprehensive adverse event reporting program. The TGA requires that a marketing authorization be submitted and reviewed for safety and efficacy, and approved before a medication can be marketed and provided to patients commercially. A separate regulatory pathway is utilized to conduct clinical trials in Australia. Australia has also an Orphan drug designation.

Regulation of Medical Devices Outside the US and Europe

In addition to regulations in the US, we will be subject to a variety of regulations in other jurisdictions governing the medical device. Whether or not we obtain FDA approval for a product and the medical device that will be used, we must obtain approval of a product and the medical device by the comparable regulatory authorities of countries outside the US before we can commence marketing of the product in those countries. The requirements for approval and the approval process vary from country to country, and the time may be longer or shorter than that required for FDA approval.

Under certain harmonized medical device approval/clearance regulations outside the US, reference to US clearance permits fast-tracking of market clearance. Other regions are harmonized with EU standards, and therefore recognize the CE mark (Conformité Européene, which means European Conformity) as a declaration of conformity to applicable standards.

Early Access Programs

European Union

Under European law, member states are authorized to adopt national legal regimes for the supply or use of non-authorized drugs in case of therapeutic needs. The most common national legal regimes are compassionate use programs and named patient sales, but other national regimes for early access may be available, depending on the member state. For drugs approved through the centralized procedure, such as orphan drugs, compassionate use programs are also regulated at the European level.

Special programs can be set up to make available to patients with an unmet medical need a promising drug which has not yet been authorized for their condition ("compassionate use"). As a general rule, compassionate use programs can only be put in place for drugs or biologics that are expected to help patients with life-threatening, long-lasting or seriously disabling illnesses who currently cannot be treated satisfactorily with authorized medicines, or who have a disease for which no medicine has yet been authorized. The compassionate use route may be a way for patients who cannot enroll in an ongoing clinical trial to obtain treatment with a potentially life-saving medicine. Compassionate use programs are coordinated and implemented by the EU member states, which decide independently how and when to open such programs according to national rules and legislation. Generally, doctors who wish to obtain a promising drug for their seriously ill patients will need to contact the relevant national authority in their respective country and follow the procedure that has been set up. Typically, the national authority keeps a register of the patients treated with the drug within the compassionate use program, and a system is in place to record any side effects reported by the patients or their doctors. Orphan drugs very often are subject to compassionate use programs due to their very nature (rare diseases are life-threatening, long-lasting or seriously disabling diseases) and the unusually long time required for both their approval and effective marketing.

Doctors can also obtain promising drugs for their patients by requesting a supply of a drug from the manufacturer or a pharmacist located in another country, to be used for an individual patient under their direct responsibility. This is often called treatment on a 'named-patient basis' and should not be confused with compassionate use programs. In this case, the doctor responsible for the

treatment will either contact the manufacturer directly or make a prescription for a pharmacist. While manufacturers or pharmacists do record what they supply, there is no central register of the patients that are being treated in this way.

Reimbursement of Pharmaceutical Products

In the US, many independent third-party payers, as well as the Medicare and state Medicaid programs, reimburse buyers of pharmaceutical products. Medicare is the federal program that provides health care benefits to senior citizens and certain disabled and chronically ill persons. Medicaid is the need-based federal and state program administered by the states to provide health care benefits to certain persons.

As one of the conditions for obtaining Medicaid and Medicare Part B coverage for our marketed pharmaceutical products, we will need to agree to pay a rebate to state Medicaid agencies that provide reimbursement for those products. We will also have to agree to sell our commercial products under contracts with the Department of Veterans Affairs, Department of Defense, Public Health Service, and numerous other federal agencies as well as certain hospitals that are designated as 340B covered entities (entities designated by federal statutes to receive drugs at discounted prices) at prices that are significantly below the price we charge to commercial pharmaceutical distributors. These programs and contracts are highly regulated and will impose restrictions on our business. Failure to comply with these regulations and restrictions could result in a loss of our ability to continue receiving reimbursement for our drugs once approved. Medicare and Medicaid programs may also seek penalties for improper marketing, including off-label marketing, of our drugs.

Private healthcare payers also attempt to control costs and influence drug pricing through a variety of mechanisms, including through negotiating discounts with the manufacturers and through the use of tiered formularies and other mechanisms that provide preferential access to certain drugs over others within a therapeutic class. Payers also set other criteria to govern the uses of a drug that will be deemed medically appropriate and therefore reimbursed or otherwise covered.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of drugs through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to patients. Some jurisdictions operate positive and negative list systems under which drugs may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other member states allow companies to fix their own prices for drugs, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new drugs. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drugs will allow favorable reimbursement and pricing arrangements for any of our products.

Regulation/Fraud and Abuse Laws

Healthcare providers, physicians and third-party payers (government or private) often play a primary role in the recommendation and prescription of health care products. In the US and most jurisdictions, numerous detailed requirements apply to government and private health care programs,

and a broad range of fraud and abuse and transparency laws are relevant to pharmaceutical companies. US federal and state healthcare laws and regulations in these areas include the following:

- The federal anti-kickback statute;
- The federal civil False Claims Act;
- The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and similar state privacy laws;
- The federal criminal false statements statute;
- The price reporting requirements under the Medicaid Drug Rebate Program and the Veterans Health Care Act of 1992;
- The federal Physician Payment Sunshine Act, being implemented as the Open Payments Program; and
- Analogous and similar state laws and regulations.

Similar restrictions apply in the member states of the European Union, which have been set out by laws or industry codes of conducts.

Employees

As of December 31, 2015, we had a total of 125 employees, including 64 in research, clinical, regulatory, medical affairs and quality assurance; 11 in technical operations, manufacturing and quality control; 36 in general and administrative functions; and 14 in pre-commercial activities. We had 114 employees in the US and 11 employees in Europe. We anticipate increasing headcount in both the US and Europe in 2016.

Our success depends in large measure on our ability to attract and retain capable executive officers and highly skilled employees who are in great demand. None of our employees are represented by a labor union and we believe that our relations with our employees are generally good. Generally, our employees are at-will employees. However, we have entered into employment agreements with certain of our executive officers.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, which we refer to as the Exchange Act. We make available on our website at http://www.insmed.com, free of charge, copies of these reports as soon as reasonably practicable after filing these reports with, or furnishing them to, the SEC. The public can also obtain materials that we file with the SEC through the SEC's website at http://www.sec.gov or at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. Information on the operation of the Public Reference Room is available by calling the SEC at 800-SEC-0330.

Also available through our website's "Investor Relations Corporate Governance" page are charters for the Audit, Compensation and Nominations and Governance committees of our board of directors, our Corporate Governance Guidelines, and our Code of Business Conduct and Ethics.

The references to our website and the SEC's website are intended to be inactive textual references only. Neither the contents of our website, nor the contents of the SEC's website, are incorporated by reference in this Annual Report on Form 10-K.

Financial Information

The financial information required under this Item 1 is incorporated herein by reference to Item 8 of this Annual Report on Form 10-K.

ITEM 1A. RISK FACTORS

Our business is subject to substantial risks and uncertainties. Any of the risks and uncertainties described below, either alone or taken together, could materially and adversely affect our business, financial condition, results of operations, prospects for growth, or the value of an investment in our common stock. In addition, these risks and uncertainties could cause actual results to differ materially from those expressed or implied by forward-looking statements contained in this Form 10-K (please read the "Cautionary Note Regarding Forward-Looking Statements" appearing at the beginning of this Form 10-K). The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial may also materially and adversely affect our business, financial condition, results of operations, prospects and the value of an investment in our common stock and could cause actual results, performance or achievements to differ materially from those expressed or implied by forward-looking statements.

Risks Related to Development and Commercialization of our Product Candidates

Our near term prospects are highly dependent on the success of our most advanced product candidate, ARIKAYCE. If we are unable to successfully complete the development of, obtain regulatory approval for, and successfully commercialize ARIKAYCE, our business and the value of our common stock may be materially adversely affected.

We are investing substantially all of our efforts and financial resources in the development of ARIKAYCE, our most advanced product candidate. Our ability to generate product revenue from ARIKAYCE will depend heavily on the successful completion of development of, receipt of regulatory approval for, and commercialization of, ARIKAYCE.

Positive results from preclinical studies of a drug candidate may not be predictive of similar results in human clinical trials, and promising results from earlier clinical trials of a drug candidate may not be replicated in later clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in earlier stages of development. Accordingly, the results of the completed clinical trials for ARIKAYCE may not be predictive of the results we may obtain in our clinical trials currently in progress or other trials.

We are conducting a global phase 3 clinical study of ARIKAYCE (the 212 or CONVERT study) in adult non-CF patients with NTM lung infections caused by MAC that are refractory to treatment. The CONVERT study is designed to confirm the culture conversion results seen in our phase 2 clinical trial (the 112 study).

In the fourth quarter of 2014, we filed an MAA with the EMA seeking approval of ARIKAYCE in the EU for the treatment of NTM lung infections based on the data from the 112 study. In February 2015 the EMA validated our MAA for ARIKAYCE for NTM lung infections, as well as cystic fibrosis (CF) patients with *Pseudomonas* lung infections. The EMA subsequently requested additional information with respect to the CF indication with respect to the similarity of ARIKAYCE to another product that has an orphan designation for the same indication. In the third quarter of 2015, the EMA adopted our request to withdraw the *Pseudomonas* indication from our MAA. We will only seek approval of ARIKAYCE for the treatment of patients with refractory NTM lung infections caused by MAC.

In December 2015, we submitted our responses to the EMA's 120-day questions and expect to receive the EMA's 180-day list of outstanding issues (the LOI) in the first quarter of 2016. We

anticipate responding to the LOI and participating in an oral hearing with the CHMP in the second quarter of 2016 to address the LOI. We continue to expect the CHMP to render an opinion around the middle of 2016. There can be no assurance, however, that results from the 112 study will be sufficient to obtain full or conditional marketing approval for ARIKAYCE. If major objections raised during the review procedure are not subsequently resolved, it may impact our ability to obtain an approval without submission of additional study data. Further, even if we obtain conditional approval, it may be withdrawn under certain circumstances and confirmatory clinical studies may be required and could fail to demonstrate sufficient safety and efficacy to obtain full approval.

We do not expect ARIKAYCE or any other drug candidates we may develop to be commercially available in any market until we get requisite approval from the EMA, FDA or equivalent regulatory agency.

We have not completed the research and development stage of ARIKAYCE or any other product candidates other than IPLEX, which we no longer market. If we are unable to successfully commercialize ARIKAYCE or any other products, it may materially adversely affect our business, financial condition, results of operations and our prospects.

Our long-term viability and growth depend on the successful commercialization of ARIKAYCE and potentially other product candidates that lead to revenue and profits. Pharmaceutical product development is an expensive, high risk, lengthy, complicated, resource intensive process. In order to conduct the development programs for our products, we must, among other things, be able to successfully:

- Identify potential drug product candidates;
- Design and conduct appropriate laboratory, preclinical and other research;
- Submit for and receive regulatory approval to perform clinical studies;
- Design and conduct appropriate preclinical and clinical studies according to good laboratory and good clinical practices and disease-specific expectations of FDA and other regulatory bodies;
- Select and recruit clinical investigators;
- Select and recruit subjects for our studies;
- Collect, analyze and correctly interpret the data from our studies;
- Submit for and receive regulatory approvals for marketing;
- Submit for and receive reimbursement approvals for market access: and
- Manufacture the drug product candidates and device components according to cGMP.

The development program with respect to any given product will take many years and thus delay our ability to generate profits. In addition, potential products that appear promising at early stages of development may fail for a number of reasons, including the possibility that the products may require significant additional testing or turn out to be unsafe, ineffective, too difficult or expensive to develop or manufacture, too difficult to administer or unstable. If we do not proceed with the development of our ARIKAYCE program in the NTM or CF indications, certain organizations that provided funding to us for such developmental efforts may elect to proceed with the development of these indications. Even if we are successful in obtaining regulatory approval for our product candidates, including ARIKAYCE, we may not obtain labeling that permits us to market them with commercially viable claims because the final wording of the approved indication may be restrictive, or the available clinical data may not provide adequate comparative data with other products. Failure to successfully commercialize our products will adversely affect our business, financial condition, results of operations and prospects.

If regulatory agencies limit our proposed NTM treatment population for ARIKAYCE, our clinical studies do not produce positive results or our clinical trials are delayed, or if serious side effects are identified during drug development, we may experience delays, incur additional costs and ultimately be unable to commercialize our product candidates in the US, Europe or other countries.

Before obtaining regulatory approval for the sale of our product candidates, we must conduct, at our own expense, extensive preclinical tests to demonstrate the safety of our product candidates in animals, and clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Significant preclinical or clinical trial delays also could shorten the patent protection period during which we may have the exclusive right to commercialize our product candidates. Such delays could allow our competitors to bring products to market before we do and impair our ability to commercialize our products or product candidates.

Preclinical and clinical testing is expensive, difficult to design and implement and can take many years to complete. Special challenges can arise in conducting trials in diseases or conditions with small populations, such as difficulties enrolling adequate numbers of patients. Our product development costs have and may continue to increase if we experience further delays in testing or approvals. A failure of one or more of our preclinical studies or clinical trials can occur at any stage of testing. We may experience numerous unforeseen events during, or as a result of, preclinical testing and the clinical trial process that could delay or prevent our ability to obtain regulatory approval or commercialize our product candidates, including:

- Our preclinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical testing or clinical trials or we may abandon projects that we expect to be promising;
- Regulators or institutional review boards may prevent us from commencing a clinical trial or conducting a clinical trial at a prospective trial site;
- Enrollment in the clinical trials may take longer than expected or the clinical trials as designed may not allow for sufficient patient accrual to complete enrollment of the trial;
- We may decide to limit or abandon our commercial development programs;
- Conditions imposed on us by the FDA or any non-US regulatory authority regarding the scope or design of our clinical trials may require us to collect and submit information to regulatory authorities, ethics committees, institutional review boards or others for review and approval;
- The number of patients required for our clinical trials may be larger than we anticipate or participants may drop out of our clinical trials at a higher rate than we anticipate;
- Our third party contractors, contract research organizations, which we refer to as CROs, clinical investigators, clinical laboratories, product supplier or inhalation device supplier may fail to comply with regulatory requirements or fail to meet their contractual obligations to us in a timely manner;
- We may have to suspend or terminate one or more of our clinical trials if we, the regulators or the institutional review boards determine that the participants are being exposed to unacceptable health risks or for other reasons;
- We may not be able to claim that a product candidate provides an advantage over current standard of care or future competitive therapies in development because our clinical studies may not have been designed to support such claims;
- Regulators or institutional review boards may require that we hold, suspend or terminate clinical research for various reasons, including potential safety concerns or noncompliance with regulatory requirements;
- The cost of our clinical trials may be greater than we anticipate;

- The supply or quality of product used in clinical trials or other materials necessary to conduct our clinical trials may be insufficient or inadequate or we may not be able to reach agreements on acceptable terms with prospective contract manufacturers or CROs; and
- The effects of our product candidates may not be the desired effects or may include undesirable side effects or the product candidates may have other unexpected characteristics.

For example, results from our rodent carcinogenicity study showed that when rats were given ARIKAYCE daily by inhalation for two years, two of the 120 rats receiving the highest dose developed lung carcinomas. These rats received ARIKAYCE doses that were within two-fold of those in clinical studies (normalized on a body surface area basis or a lung weight basis). Based on these results, in 2011 the FDA placed clinical holds on our phase 3 clinical trials for ARIKAYCE, which holds were lifted in 2012. In 2013, we concluded a nine month dog inhalation toxicity study. The final report from the study stated that the lung macrophage response in dogs was similar to that seen in our previous three month dosing dog study, and there was no evidence of neoplasia, squamous metaplasia or proliferative changes. However, approvability or labeling of ARIKAYCE may still be negatively affected by the prior results from the rat carcinogen study.

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 our clinical trials 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, or may not be able to obtain, marketing approval for one or more of our product candidates;
- Obtain approval for indications that are not as broad as intended or entirely different than those indications for which we sought approval; or
- Have the product removed from the market after obtaining marketing approval.

We may not have, or may be unable to obtain, sufficient quantities of our product candidates to meet our required supply for clinical studies or commercialization requirements.

We do not have any in-house manufacturing capability other than for development and characterization and depend completely on a small number of third-party manufacturers and suppliers for the manufacture of our product candidates on a clinical or commercial scale. We are currently dependent on Althea for the production of ARIKAYCE. In September 2015, we entered into a Commercial Fill/Finish Services Agreement with Althea to produce ARIKAYCE on a non-exclusive basis. Althea currently manufactures ARIKAYCE at a relatively small scale. In order to meet potential commercial demand, we have constructed a manufacturing operation at Therapure in Canada as an alternate site of manufacture that operates at a larger scale. Our supply of the active pharmaceutical ingredient for INS1009 is dependent on a single supplier. The inability of a supplier to fulfill our supply requirements could materially adversely affect our ability to obtain and maintain regulatory approvals and future operating results. A change in the relationship with any supplier, or an adverse change in their business, could materially adversely affect our future operating results.

We are dependent upon Althea and Therapure being able to provide an adequate supply of ARIKAYCE both for our clinical trials and for commercial sale in the event ARIKAYCE receives marketing approval. We intend to work closely with Althea and Therapure to coordinate efforts regarding regulatory requirements and our supply needs.

We are dependent upon PARI being able to provide an adequate supply of nebulizers both for our clinical trials and for commercial sale in the event ARIKAYCE receives marketing approval. PARI

is the sole manufacturer of the eFlow nebulizer system. These nebulizers must be in good working order and meet specific performance characteristics. We intend to work closely with PARI to coordinate efforts regarding regulatory requirements.

We do not have long-term commercial agreements with all of our suppliers and if any of our suppliers are unable or unwilling to perform for any reason, we may not be able to locate suppliers or enter into favorable agreements with them. Any inability to acquire sufficient quantities of our components in a timely manner from these third parties could delay clinical trials or commercialization and prevent us from developing and distributing our products in a cost-effective manner or on a timely basis.

In addition, manufacturers of our components are subject to cGMP and similar standards and we do not have control over compliance with these regulations by our manufacturers. If one of our contract manufacturers fails to maintain compliance, the production of our products could be interrupted, resulting in delays and additional costs. In addition, if the facilities of such manufacturers do not pass a pre-approval or post-approval plant inspection, the FDA, as well as other regulatory authorities in jurisdictions outside the US, will not grant approval and may institute restrictions on the marketing or sale of our products. We are reliant on third-party manufacturers and suppliers to meet our clinical supply demands and any future commercial products. Delays in receipt of materials, scheduling, release, custom's control and regulatory compliance issues may adversely impact our ability to initiate, maintain or complete clinical trials that we are sponsoring or may adversely impact commercialization. Issues arising from scale-up, facility construction, environmental controls, equipment requirements, local and federal permits and allowances or other factors may have an adverse impact on our ability to manufacture our product candidates.

We have limited experience in conducting and managing the preclinical development activities and clinical trials necessary to obtain regulatory approvals, including approval by the FDA and EMA and other regulatory agencies.

We have limited experience in conducting and managing the preclinical development activities and clinical trials necessary to obtain regulatory approvals, including approval by the FDA and EMA. Since our merger with Transave, we have not completed a regulatory filing and review process for, obtained regulatory approval of or commercialized any of our product candidates. Our limited experience might prevent us from successfully designing, implementing, or completing a clinical trial. The application processes for FDA, EMA and other regulatory agencies are complex and difficult and vary by regulatory agency. We have limited experience in conducting and managing the application processes necessary to obtain regulatory approvals in the various countries and we might not be able to demonstrate that our product candidates meet the appropriate standards for regulatory approval. If we are not successful in conducting and managing our preclinical development activities or clinical trials or obtaining regulatory approvals, we might not be able to commercialize ARIKAYCE, or might be significantly delayed in doing so, which may materially harm our business.

We may not be able to enroll enough patients to complete our clinical trials.

The completion rate of our global phase 3 clinical study of ARIKAYCE for NTM and other future clinical studies of our products is dependent on, among other factors, the patient enrollment rate. Patient enrollment is a function of many factors, including:

- Investigator identification and recruitment;
- Regulatory approvals to initiate study sites;
- Patient population size;

- The nature of the protocol to be used in the trial;
- Patient proximity to clinical sites;
- Eligibility criteria for the study;
- The patients' willingness to participate in the study;
- Competition from other companies' potential clinical studies for the same patient population; and
- Ability to obtain any necessary comparator drug or medical device.

While we believe our procedures for enrolling patients to date have been appropriate, enrollment at certain centers is slower than expected. As a result, we expect to achieve our enrollment objective six to twelve months later than our initial expectation and now expect to enroll the study by the end of 2016. While we have taken a number of steps to accelerate enrollment, there is no guarantee that our enrollment will be completed by the expected time. Delays in patient enrollment for future clinical trials could increase costs and delay ultimate commercialization and sales, if any, of our products.

If any of our products meet the criteria for approval pursuant to Subpart H (accelerated approval), such approval will be subject to our carrying out, with due diligence, adequate and well-controlled post market studies to verify and describe their clinical benefit. If we fail to complete such studies with due diligence, or if the results of such studies fail to demonstrate clinical benefit, FDA may, following a hearing, withdraw product approval.

The commercial success of ARIKAYCE or any other product candidates that we may develop will depend upon many factors, including the degree of market acceptance by physicians, patients, third-party payers and others in the medical community.

Even if we are able to successfully complete development of, obtain regulatory approval for, and bring ARIKAYCE to market, ARIKAYCE may not gain market acceptance by physicians, patients, third-party payers and others in the medical community. If ARIKAYCE, or any other products we bring to market, 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 ARIKAYCE and any other product candidates, if approved for commercial sale, will depend on a number of factors, including:

- The prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- The efficacy and potential advantages over alternative treatments;
- The pricing of our product candidates;
- Relative convenience and ease of administration;
- The willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- The strength of marketing and distribution support and timing of market introduction of competitive products;
- Publicity concerning our products or competing products and treatments, including competing products becoming subject to generic pricing; and
- Sufficient third party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical and clinical trials, market acceptance of the product will not be known until after it is launched. For example, if a clinical trial is not designed to demonstrate advantages over alternative treatments, we may be prohibited from promoting our product candidates on any such advantages. Our efforts to

educate the medical community and third-party payers on the benefits of our product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by more established technologies marketed by our competitors.

We currently have a very small marketing or sales organization, and we have limited experience as a company in marketing drug products. If we are unable to establish our own marketing and sales capabilities, or are unable to enter into agreements with third parties, to market and sell our products after they are approved, we may not be able to generate product revenues.

We have a small commercial organization for the marketing, market access, sales and distribution of any drug products. In order to commercialize ARIKAYCE or any other product candidates, we must develop these capabilities on our own or make arrangements with third parties for the marketing, sales and distribution of our products. During 2015, we started to build our EU commercial infrastructure to support the launch of ARIKAYCE in certain countries in Europe, if approved. The establishment and development of our own sales force would be expensive and time consuming and could delay any product launch, and we cannot be certain that we would be able to successfully develop this capability. As a result, we may seek one or more partners to handle some or all of the sales and marketing of ARIKAYCE in certain markets. However, we may not be able to enter into arrangements with third parties to sell ARIKAYCE on favorable terms or at all. In the event we are unable to develop our own marketing, market access, and sales force or collaborate with a third-party marketing, market access, and sales organization, we may not be able to successfully commercialize ARIKAYCE or any other product candidates that we develop, which would adversely affect our ability to generate product revenues. Further, whether we commercialize products on our own or rely on a third party to do so, our ability to generate revenue will be dependent on the effectiveness of the sales force.

Promotional materials for our approved drug products must be submitted, along with Form 2253, to FDA's Office of Prescription Drug Products (OPDP) at the time of initial dissemination or publication. For products approved pursuant to 21 CFR 314 Subpart H, promotional materials intended to be used during product launch must be submitted during the pre-approval review period, and thereafter must be submitted at least 30 days prior to the intended time of initial dissemination or publication. For other products, OPDP encourages pre-launch review, and will provide advisory comments in response to such submissions upon request. There is no guarantee that OPDP will agree that the proposed promotional materials comply with applicable FDA requirements. A negative response in OPDP Advisory Comments may require us to revise planned promotional materials and may limit the claims we can use in such materials. If OPDP considers promotional materials already disseminated or published to violate applicable FDA requirements, OPDP may initiate enforcement action, including Untitled Letters (previously known as Notices of Violation), Warning Letters, Injunction/Consent decree, Seizures, Criminal prosecution, and/or civil and monetary penalties.

We have limited experience operating internationally, are subject to a number of risks associated with our international activities and operations and may not be successful in our efforts to expand internationally.

We have manufacturing, collaboration, clinical trial and other relationships outside the US but we currently have limited operations outside of the US. Specifically, as of December 31, 2015, we had 11 employees located in Europe and we expect that number to grow in 2016 and beyond as we prepare for commercialization in Europe. In order to meet our long-term goals, we will need to grow our international operations over the next several years. Consequently, we are and will continue to be subject to additional risks related to operating in foreign countries, including:

- we have limited experience operating our business internationally;

- we may not achieve the optimal pricing and reimbursement for ARIKAYCE;
- there may be fewer addressable NTM patients than were originally forecasted;
- unexpected adverse events related to ARIKAYCE or our other product candidates that occur in foreign markets that we have not experienced in the US;
- local, economic and political conditions, including geopolitical events, such as war and terrorism, foreign currency fluctuations, which could result in increased or unpredictable operating expenses and reduced revenues and other obligations incident to doing business in, or with a company located in, another country;
- unexpected changes in reimbursement and pricing requirements, tariffs, trade barriers and regulatory requirements;
- economic weakness, including foreign currency exchange risks, inflation or political instability in particular foreign economies and markets; and
- compliance with foreign or US laws, rules and regulations, including data privacy requirements, labor relations laws, tax laws, anti-competition regulations, import, export and trade restrictions, anti- bribery/anti-corruption laws, regulations or rules, which could lead to actions by us or our licensees, distributors, manufacturers, other third parties who act on our behalf or with whom we do business in foreign countries or our employees who are working abroad that could subject us to investigation or prosecution under such foreign or US laws.

These and other risks associated with our international operations may materially adversely affect our business and results of operations.

Risks Related to Our Reliance on Third Parties

We rely on third parties including clinical research organizations, or CROs, clinical laboratories, analytical laboratories and other providers for many services. If we are unable to form and sustain these relationships, or if any third-party arrangements that we may enter into are unsuccessful, our ability to develop and commercialize our products may be materially adversely affected.

We currently rely, and expect that we will in the future continue to rely, on third parties for significant research, analytical services, preclinical development and clinical development. For example almost all of our clinical trial work is done by CROs, such as Synteract who is our CRO for both the 212 and 312 studies, and clinical laboratories. Reliance on these third parties poses a number of risks, including the following:

- We may face significant competition in seeking appropriate partners;
- These arrangements are complex and time consuming to negotiate, document and implement;
- We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements that we might pursue on favorable terms;
- We may not be able to effectively control whether the CROs or other third parties will devote sufficient resources to our programs or products;
- We are not able to control the regulatory compliance of CROs, third-party suppliers, contractors and collaborators, including their processes and procedures, systems utilized to collect and analyze data, and equipment used to test drug product and/or clinical supplies;
- Disagreements with third parties and CROs may be difficult to resolve and could result in a dispute over and loss of intellectual property rights, delay or termination of the research, development, or commercialization of product candidates or result in litigation or arbitration;
- Contracts with our collaborators may fail to provide sufficient protection of our intellectual property; and
- We may have difficulty enforcing the contracts if one of these collaborators fails to perform.

A great deal of uncertainty exists regarding the success of any current and future third-party efforts on which we might depend. Failure of these efforts could delay, impair, or prevent the development and commercialization of our products and adversely affect our business, financial condition, results of operations and prospects.

We rely on PARI, a third party manufacturer, to supply the nebulizer that is used for ARIKAYCE. Any disruption in supply of the nebulizer will have a material adverse effect on our business.

We are dependent upon PARI being able to provide an adequate supply of nebulizers both for our clinical trials and for commercial sale in the event ARIKAYCE receives marketing approval. These nebulizers must be in good working order, meet specific performance characteristics and be approved by FDA and other regulatory agencies along with ARIKAYCE. We have no alternative supplier for the nebulizer and we do not intend to seek an alternative or secondary supplier of nebulizers. Significant effort and time were expended in the optimization of the nebulizer for use with ARIKAYCE. In the event PARI cannot provide devices, replication of the optimized device by another party may require considerable time and additional regulatory approval. In the case of certain defined supply failures, we will have the right under the PARI Agreement to make the Device and have it made by third parties, but not certain third parties deemed under the PARI Agreement to compete with PARI. PARI has the right to terminate this agreement upon written notice for our uncured material breach, or if we are the subject of specified bankruptcy or liquidation events. In the event PARI terminates the supply agreement and ceases to manufacture the nebulizer, we cannot be certain that we would be able identify another willing supplier for the nebulizer on terms we require. A disruption in the supply of nebulizers could delay, impair, or prevent the development and commercialization of our products and adversely affect our business, financial condition, results of operations and prospects.

We rely on Ajinomoto Althea, Inc. and Therapure, third party manufacturers, to supply ARIKAYCE. Any disruption in the supply of ARIKAYCE could have a material adverse effect on our business.

We are dependent upon Ajinomoto Althea, Inc. ("Althea") to provide an adequate supply of ARIKAYCE both for our clinical trials and for commercial sale in the event ARIKAYCE receives marketing approval. In September 2015, we entered into a Commercial Fill/Finish Services Agreement with Althea to produce ARIKAYCE. Althea has the right to terminate this agreement upon written notice for our uncured material breach, if we are the subject of specified bankruptcy or liquidation events, or without cause with 24 months' prior written notice. In the event Althea terminates the supply agreement and ceases to supply ARIKAYCE, we cannot be certain that we would be able to identify another willing supplier for ARIKAYCE on terms we require or that are favorable to us. A disruption in the supply of ARIKAYCE could delay, impair, or prevent clinical trials, the development and commercialization of ARIKAYCE and adversely affect our business, financial condition, results of operations and prospects.

Althea currently manufactures ARIKAYCE at a relatively small scale. In order to meet potential commercial demand, if ARIKAYCE is approved, we have constructed a manufacturing operation at Therapure in Canada as an alternate site of manufacture that operates at a larger scale. We may not be able to obtain regulatory approvals for ARIKAYCE produced at Therapure's facility. We may not be able to secure an alternative source of ARIKAYCE at an adequate scale of production. An inadequate supply of ARIKAYCE could delay, impair, or prevent clinical trials, the development and commercialization of ARIKAYCE and adversely affect our business, financial condition, results of operations and prospects.

We currently depend on third parties to conduct the operations of our clinical trials.

We rely on third parties, such as CROs like Synteract, medical institutions, clinical investigators and contract laboratories to oversee some of the operations of our clinical trials and to perform data collection and analysis. As a result, we may face additional delays outside of our control if these parties do not perform their obligations in a timely fashion or in accordance with regulatory requirements. If these third parties do not successfully carry out their contractual duties or obligations and meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or for other reasons, our financial results and the commercial prospects for ARIKAYCE or our other potential product candidates could be materially harmed, our costs could increase and our ability to obtain regulatory approval and commence product sales could be delayed.

We also rely on third parties to select and enter into agreements with clinical investigators to conduct clinical trials to support approval of our products and the failure of these third parties to carry out such evaluation and selection can adversely affect the quality of the data from these studies and, potentially, the approval of our products. In particular, as part of our new drug approval submissions, we must disclose any financial interests of investigators who participated in any of the clinical studies being submitted in support of approval, or must certify to the absence of such financial interests. FDA evaluates the information contained in such disclosures to determine whether disclosed interests may have an impact on the reliability of a study. If FDA determines that financial interests of any clinical investigator raise serious questions of data integrity, FDA can institute a data audit, request that we submit further data analyses, conduct additional independent studies to confirm the results of the questioned study, or refuse to use the data from the questioned study as a basis for approval. A finding by FDA that a financial relationship of an investigator raises serious questions of data integrity, could delay or otherwise adversely affect approval of our products.

Risks Related to Our Financial Condition and Capital Requirements

We have a history of operating losses. We expect to incur operating losses for the foreseeable future and may never achieve or maintain profitability.

We are a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. We have incurred losses each previous year of our operation, except in 2009, when we sold our manufacturing facility and certain other assets to Merck. We expect to continue incurring operating losses for the foreseeable future. The process of developing and commercializing our products requires significant pre-clinical and clinical testing as well as regulatory approvals for commercialization and marketing before we are allowed to begin product sales. In addition, commercialization of our drug candidates likely would require us to significantly expand our sales and marketing organization and establish contractual relationships to enable product manufacturing and other related activities. We expect that our activities, together with our general and administrative expenses, will continue to result in substantial operating losses for the foreseeable future. As of December 31, 2015, our accumulated deficit was $589.0 million. For the year ended December 31, 2015, our consolidated net loss was $118.2 million.

To achieve and maintain profitability, we need to generate significant revenues from future product sales. This will require us to be successful in a range of challenging activities, including:

- Successfully completing development of and obtaining regulatory approval for the marketing of ARIKAYCE and possibly other product candidates which have yet to be developed and which would also require marketing approval;

- Commercializing ARIKAYCE and any other product candidates for which we obtain marketing approval; and
- Achieving market acceptance and reimbursement of ARIKAYCE and any other product candidates for which we obtain marketing approval in the medical community and with patients and third-party payers.

ARIKAYCE will require marketing approval and significant investment in commercial capabilities, including manufacturing and sales and marketing efforts, before its product sales can generate any revenues for us. Because of the numerous risks and uncertainties associated with drug development and commercialization, we are unable to predict the extent of any future losses. We may never successfully commercialize ARIKAYCE or any other products, generate significant future revenues or achieve and sustain profitability.

We expect that we will need additional funds in the future to continue our operations, but we face uncertainties with respect to our ability to access capital.

Our operations have consumed substantial amounts of cash since our inception. We expect to continue to incur substantial research and development expenses, and we expect to expend substantial financial resources to complete development of, seek regulatory approval for, and prepare for commercialization of ARIKAYCE. We may need to seek additional funding in order to complete any clinical trials related to ARIKAYCE, seek regulatory approvals of ARIKAYCE, and commercially launch ARIKAYCE. We also may require additional future capital in order to continue our other research and development activities or to fund corporate development. As of December 31, 2015, we had $282.9 million of cash and cash equivalents on hand. If adequate funds are not available to us when needed, we may be required to reduce or eliminate research and development programs or commercial efforts.

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

- Phase 3 clinical trials and commercialization of ARIKAYCE;
- Early access programs;
- Non-clinical and clinical testing;
- Process development and scale up for manufacturing;
- Manufacturing for clinical trials and commercial demand;
- Performance of our third-party suppliers and manufacturers;
- Obtaining marketing, sales and distribution capabilities;
- Obtaining regulatory approvals;
- Research and development, including formulation development;
- Retaining employees and consultants;
- Global expansion efforts;
- Filing and prosecuting patent applications and enforcing and defending patent claims;
- Establishing strategic alliances and collaborations with third-parties; and
- Potential future litigation.

We also may need to spend more funds than currently expected because we may further change or alter drug development plans, acquire additional drugs or drug candidates or we may misjudge our costs. As of December 31, 2015, we had no committed sources of capital and do not know whether additional financing will be available when needed, or, if available, that the terms will be favorable. We cannot assure that our cash reserves together with any subsequent funding will be sufficient for our capital requirements. The failure to satisfy our capital requirements will adversely affect our business, financial condition, results of operations and prospects.

We may seek additional funding through strategic alliances, private or public sales of our securities, debt financing or licensing all or a portion of our technology or through other means. Such funding may significantly dilute existing shareholders, subject us to contractual restrictions such as operating or financial covenants or limit our rights to our technology.

We currently have no meaningful source of revenue.

In 2015 and 2014, we generated no meaningful revenue. In 2013, we generated other revenue from the modification of a previously granted license of our IPLEX technology to Premacure. Unless we can execute one or more revenue generating transactions or successfully obtain regulatory approval for and commercialize ARIKAYCE, we will have no material sources of operating revenue. We expect to continue to incur substantial additional operating losses for at least the next several years as we continue to develop and seek to commercialize ARIKAYCE.

If we are not successful in our efforts to evaluate potential future IPLEX initiatives and to identify and engage in possible out-licensing opportunities for IPLEX, we may not derive any future revenues from IPLEX.

IPLEX is no longer a development priority for us. We no longer have protein development capability or the in-house capability to manufacture IPLEX. Accordingly, we continue to evaluate possible out-licensing opportunities for IPLEX. We may have difficulty identifying possible markets, and securing prospective partners for out-licensing, including as a result of certain opt-in and other rights retained by Ipsen and Genentech related to future development of IPLEX pursuant to the patent infringement settlement agreement among us, Ipsen and Genentech. Even if we are able to enter into out-licensing arrangements, we may not derive any revenue from those arrangements.

Our loan agreement with Hercules Technology Growth Capital, Inc. ("Hercules") contains covenants that impose restrictions on our operations that may adversely affect our ability to optimally operate our business or to maximize shareholder value.

Our loan agreement with Hercules contains various restrictive covenants, including restrictions on our ability to incur additional debt, transfer or place a lien or security interest on our assets, including our intellectual property, merge with or acquire other companies, redeem or repurchase any shares of our capital stock or pay cash dividends to our stockholders. The loan agreement also contains certain other covenants (including limitations on other indebtedness, liens, acquisitions, investments and dividends), and events of default (including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of the lender's security interest or in the collateral, and events relating to bankruptcy or insolvency). Upon the occurrence of an event of default, a default interest rate of an additional 5% may be applied to the outstanding loan balances, and the lender may terminate its lending commitment, declare all outstanding obligations immediately due and payable, and take such other actions as set forth in the Loan Agreement. In addition, pursuant to the Loan Agreement, the lender has the right to participate, in an amount of up to $1.0 million, in certain future private equity financing(s).

Under our loan agreement with Hercules, we have borrowed $25.0 million as of December 31, 2015, bearing interest of 9.25%. In December 2015, we completed an amendment of our loan agreement by exercising an option to extend the maturity date to January 1, 2018 with a payment to Hercules of $250,000. The amendment extend the interest-only period, with principal repayments beginning in October 2016. Our borrowings under the Loan Agreement are secured by a lien on our assets, excluding our intellectual property, and in the event of a default on the loan, the lender may have the right to seize our assets securing our obligations under the Loan Agreement. The terms and restrictions provided for in the Loan Agreement may inhibit our ability to conduct our business and to

provide distributions to our stockholders. Future debt securities or other financing arrangements could contain negative covenants similar to, or even more restrictive than, the Hercules loan.

In process research and development (IPRD) currently comprises approximately 16% of our total assets. A reduction in the value of our IPRD could impact our results of operations and financial condition.

As a result of the merger with Transave in 2010 we recorded an intangible IPRD asset of $77.9 million and goodwill of $6.3 million on our balance sheet. As a result of our clinical hold announced in late 2011 we recorded a charge of $26.0 million in the fourth quarter of 2011 and reduced the value of IPRD to $58.2 million and reduced goodwill to zero. Other potential future activities or results could result in additional write-downs of IPRD, which would adversely affect our results of operations and financial condition.

We may be unable to use our net operating losses.

We have substantial tax loss carry forwards for US federal income tax purposes and beginning in 2015, we have tax losses in Ireland as well. Our ability to fully use certain US tax loss carry forwards prior to December 2010 to offset future income or tax liability was limited under section 382 of the Internal Revenue Code of 1986, as amended. Changes in the ownership of our stock, including those resulting from the issuance of shares of our common stock upon exercise of outstanding options, may limit or eliminate our ability to use certain net operating losses in the future.

Any acquisitions we make, or collaborative relationships we enter into, may require a significant amount of our available cash and may not be scientifically or commercially successful.

As part of our business strategy, we may effect acquisitions to obtain additional businesses, products, technologies, capabilities and personnel. Nonetheless, we cannot assure you that we will identify suitable products or enter into such acquisitions on acceptable terms. If we make one or more significant acquisitions in which the consideration includes cash, we may be required to use a substantial portion of our available cash and/or need to raise additional capital.

Acquisitions involve a number of operational risks, including:

- failure to achieve expected synergies;
- difficulty and expense of assimilating the operations, technology and personnel of the acquired business;
- our inability to retain the management, key personnel and other employees of the acquired business;
- our inability to maintain the acquired company's relationship with key third parties, such as alliance partners;
- exposure to legal claims for activities of the acquired business prior to the acquisition;
- the diversion of our management's attention from our core business; and
- the potential impairment of goodwill and write-off of in-process research and development costs, adversely affecting our reported results of operations and financial condition.

We also may enter into collaborative relationships that would involve our collaborators conducting proprietary development programs. Any conflict with our collaborators could limit our ability to obtain future collaboration agreements and negatively influence our relationship with existing collaborators. Disagreements with collaborators may also develop over the rights to our intellectual property.

Risks Related to Regulatory Matters

We may not be able to obtain regulatory approvals for ARIKAYCE or any other products we develop in the US, Europe or other countries. If we fail to obtain such approvals, we will not be able to commercialize our products.

We are required to obtain various regulatory approvals prior to studying our products in humans and then again before we market and distribute our products. The regulatory review and approval processes in both the US and Europe require evaluation of preclinical studies and clinical studies, as well as the evaluation of our manufacturing process. These processes are complex, lengthy, expensive, resource intensive and uncertain. Securing regulatory approval to market our products requires the submission of much more extensive preclinical and clinical data, manufacturing information regarding the process and facility, scientific data characterizing our product and other supporting data to the regulatory authorities in order to establish its safety and effectiveness. This process also is complex, lengthy, expensive, resource intensive and uncertain. We have limited experience in submitting and pursuing applications necessary to gain these regulatory approvals.

Data submitted to the regulators is subject to varying interpretations that could delay, limit or prevent regulatory agency approval. We may also encounter delays or rejections based on changes in regulatory agency policies during the period in which we develop a product and the period required for review of any application for regulatory agency approval of a particular product. For example, FDA has designated ARIKAYCE for Fast Track, Breakthrough Therapy and QIDP status, all programs intended to expedite or streamline the development and regulatory review of the drug. If we were to lose the current designation under one or more of those programs, we could face delays in the FDA review and approval process. Even with these designations, there is no guarantee we will receive approval for ARIKAYCE on a timely basis, or at all.

The Generating Antibiotic Incentives Now (GAIN) Act established incentives for the development of new therapies for serious and life-threatening infections by making streamlined priority review and fast track processes available for drugs which the FDA designates as QIDPs. To qualify for designation as a QIDP according to the criteria established in the GAIN Act a product must be an antibacterial or anti-fungal drug for human use intended to treat serious or life-threatening infections, including: those caused by an anti-fungal resistant pathogen, including novel or emerging infectious pathogens; or caused by qualifying pathogens listed by the FDA in accordance with the GAIN Act. Under the fast track program generally, the sponsor of an IND may request FDA to designate the drug candidate as a fast track drug if it is intended to treat a serious condition and fulfill an unmet medical need. FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request. Once FDA designates a drug as a fast track candidate, it is required to facilitate the development and expedite the review of that drug by providing more frequent communication with and guidance to the sponsor.

Delays in obtaining regulatory agency approvals could adversely affect the development and marketing of any drugs that we or any third parties develop. Resolving such delays could force us or third parties to incur significant costs, could limit our allowed activities or the allowed activities of third parties, could diminish any competitive advantages that we or our third parties may attain or could adversely affect our ability to receive royalties, any of which could materially adversely affect our business, financial condition, results of operations or prospects.

To market our products outside of the US and, Europe, we and any potential third parties must comply with numerous and varying regulatory requirements of other countries. The approval procedures vary among countries and can involve additional product testing and administrative review

periods. The time required to obtain approval in these other territories might differ from that required to obtain FDA or EMA approval. The regulatory approval process in these other territories includes at least all of the risks associated with obtaining FDA and EMA approval detailed above.

Specifically related to INS1009, we believe that this product could be eligible for approval under Section 505(b)(2) of the FDCA. Like a traditional NDA that is submitted under Section 505(b)(1) of the FDCA, a 505(b)(2) NDA must establish that the drug is safe and effective, but unlike a traditional NDA the applicant may rely at least in part on studies not conducted by or for the applicant and for which the applicant does not have a right of reference. The ability to rely on existing data to support safety and/or effectiveness can reduce the time and cost associated with traditional NDAs. We cannot be sure that we will obtain approval for INS1009 under the 505(b)(2) pathway.

Approval by the FDA or the EMA does not ensure approval by the regulatory authorities of other countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. In addition, we may be subject to fines, suspension or withdrawal of marketing approvals, product recalls, seizure of products, operating restrictions and criminal prosecution if we fail to comply with applicable US and foreign regulatory requirements. If we fail to comply with regulatory requirements or to obtain and maintain required approvals, our target market may be reduced and our ability to realize the full market potential of our product candidates may be harmed. The failure to obtain such approvals may materially adversely affect our business, financial condition, results of operations and our prospects.

There is little or no precedent for clinical development and regulatory expectations for agents to treat NTM; as a result we may encounter challenges developing clinical endpoints that will ultimately be satisfactory to regulators, and may need to reevaluate our surrogate endpoints at various points in time.

FDA may base accelerated approval for drugs for serious conditions that fill an unmet medical need on whether the drug has an effect on a surrogate or an intermediate clinical endpoint (other than survival or irreversible morbidity). FDA regulations referred to as "Subpart H—Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses" describe the potential use of surrogate endpoints. A surrogate endpoint used for accelerated approval is a marker—a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Likewise, an intermediate clinical endpoint is a measure of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on irreversible morbidity and mortality. The FDA bases its decision on whether to accept the proposed surrogate or intermediate clinical endpoint on the scientific support for that endpoint. Studies that demonstrate a drug's effect on a surrogate or intermediate clinical endpoint must be "adequate and well controlled" as required by the FD&C Act.

If a drug is approved based on a surrogate endpoint under Subpart H the approval will be subject to the requirement that the applicant study the drug further, to verify and describe its clinical benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to the ultimate outcome. Post marketing studies would usually be studies already underway. When required to be conducted, such studies must also be adequate and well-controlled. The applicant shall carry out any such studies with due diligence. Developing clinical endpoints that are unsatisfactory to regulators could delay clinical trials and the FDA approval process which could materially adversely affect our business, financial condition, results of operations and our prospects.

In addition, even if we are successful in obtaining accelerated approval in the US or under comparable pathways in other jurisdictions, we may face requirements and limitations that will adversely affect our commercial prospects. For example, we may not successfully complete required post-approval trials, or such trials may not confirm the clinical benefit of our drug, and we may be required to withdraw approval of the drug.

For ARIKAYCE to be successfully developed and commercialized, in addition to regulatory approvals required for ARIKAYCE, the eFlow nebulizer system must satisfy certain regulatory requirements and its use as a delivery system for ARIKAYCE must be approved for use in any market in which we intend to commercialize ARIKAYCE.

Although the optimized eFlow Nebulizer System is CE marked by PARI in Europe, outside Europe it is labeled as investigational for use in our clinical trials in the US, Canada, Australia and Japan. The optimized eFlow Nebulizer System is not approved for commercial use in the US, Canada or certain other markets in which we may choose to commercialize ARIKAYCE if approved. The eFlow Nebulizer System must receive regulatory approval before we can market ARIKAYCE. We will continue to work closely with PARI to coordinate efforts regarding regulatory requirements, including our proposed filings for a drug and device. However, we or PARI may not be successful in meeting the regulatory requirements for the eFlow Nebulizer System, which could prevent or hinder our ability to bring ARIKAYCE to market or market it successfully.

Even if we obtain marketing approval for ARIKAYCE or any of our other product candidates, we will continue to face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if marketing approval in the US is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing, including risk evaluation and mitigation strategies, or may impose ongoing requirements on us, including with respect to:

- Labeling, such as black box or other warnings or contraindications;
- Post-market surveillance, post-market studies or post-market clinical trials;
- Packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post-market information;
- Monitoring and reporting adverse events and instances of the failure of a product to meet the specifications in the NDA;
- Changes to the approved product, product labeling or manufacturing process;
- Advertising and other promotional material; and
- Disclosure of clinical trial results on publicly available databases.

In addition, the third-party manufacturers of our products and their facilities are and will be subject to continual review and periodic inspections by the FDA and other regulatory authorities. The distribution, sale and marketing of our products are subject to a number of additional requirements, including:

- State wholesale drug distribution laws and the distribution of our product samples to physicians must comply with the requirements of the Prescription Drug Marketing Act;
- Sales, marketing and scientific or educational grant programs must comply with the anti-kickback and fraud and abuse provisions of the Social Security Act, the transparency provision of the Patient Protection and Affordable Care Act and an associated reconciliation bill that became law in March 2010, which we refer to collectively as the Health Care Reform Law, federal and state patient privacy laws, the False Claims Act and similar state laws; and

- Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veteran's Health Care Act of 1992, and if products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply.

All of these activities also may be subject to federal and state consumer protection and unfair competition laws.

We also are subject to changes or revisions to these laws and regulations that may make gaining regulatory approval, reimbursement and pricing more difficult or at least subject to different criteria and standards.

If we or any third party involved in our manufacturing or commercialization efforts fail to comply with applicable regulatory requirements, a regulatory agency may:

- Issue warning letters or untitled letters asserting that we are in violation of the law;
- Seek an injunction or impose civil or criminal penalties or monetary fines;
- Suspend or withdraw marketing approval;
- Suspend any ongoing clinical trials;
- Refuse to approve pending applications or supplements to applications submitted by us;
- Suspend or impose restrictions on operations, including costly new manufacturing requirements;
- Seize or detain products, refuse to permit the import or export of products, or require us to initiate a product recall;
- Refuse to allow us to enter into supply contracts, including government contracts;
- Impose civil monetary penalties; or
- Pursue civil or criminal prosecutions and fines against our company or responsible officers.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenues.

Even if we obtain marketing approval for ARIKAYCE or any of our other product candidates, adverse effects discovered after approval could limit the commercial profile of any approved product.

If we obtain marketing approval for ARIKAYCE or any other product candidate that we develop, such products will be used by a larger number of patients and for longer periods of time than they were used in clinical trials. For these reasons or other reasons, we or others may later discover that our products have adverse effect profiles that limit their usefulness or require their withdrawal. This discovery could have a number of potentially significant negative consequences, including:

- Regulatory authorities may withdraw their approval of the product and may require recall of product in distribution;
- Regulatory authorities may require the addition of labeling statements, such as black box or other warnings or contraindications;
- Regulatory authorities may require us to issue specific communications to healthcare professionals, such as "Dear Doctor Letters;"
- Regulatory authorities may impose additional restrictions on marketing and distribution of the products, or other risk management measures;

- Regulatory authorities may issue negative publicity regarding the product, including safety communications;
- We may be required to change the way the product is administered, conduct additional clinical studies or restrict the distribution of the product;
- We could be sued and held liable for harm caused to subjects;
- We could be subject to negative publicity; and
- Our reputation may suffer.

Any of these events could prevent us from maintaining market acceptance of the affected product, could cause substantial reduction of sales, could substantially increase the costs of commercializing our product candidates, and could cause significant financial losses.

If we are unable to obtain adequate reimbursement from governments or third-party payers for ARIKAYCE or any other products that we may develop or if we are unable to obtain acceptable prices for those products, our prospects for generating revenue and achieving profitability may be materially adversely affected.

Our prospects for generating revenue and achieving profitability depend heavily upon the availability of adequate reimbursement for the use of our approved product candidates from governmental and other third-party payers, both in the US and in other markets. Reimbursement by a third party payer may depend upon a number of factors, including the third party payer's determination that use of a product is:

- A covered benefit under its health plan;
- Safe, effective and medically necessary;
- Appropriate for the specific patient;
- Cost-effective; and
- Neither experimental nor investigational.

Obtaining reimbursement approval for a product from each government or other third-party payer is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to each payer. We may not be able to provide data sufficient to gain acceptance with respect to reimbursement or we might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payers' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Even when a payer determines that a product is eligible for reimbursement, the payer may impose coverage limitations that preclude payment for some uses that are approved by the FDA or non-US regulatory authorities. In addition, there is a risk that full reimbursement may not be available for high priced products. Moreover, eligibility for coverage does not imply that any product will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs. Interim payments for new products, if applicable, also may not be sufficient to cover our costs and may not be made permanent. Subsequent approvals of competitive products could result in a detrimental change to the reimbursement of our products.

There is a significant focus in the US healthcare industry and elsewhere on cost containment and value. We expect changes in the Medicare program and state Medicaid programs, as well as managed care organizations and other third-party payers to continue to put pressure on pharmaceutical product pricing in return for near-term cost effectiveness or budget impact. In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare outpatient prescription drug coverage for the elderly through Part D prescription drug plans sponsored by private entities. The legislation authorized such plans to use formularies where they can limit the

number of drugs that will be covered in any therapeutic class. The plans generally negotiate significant price concessions as a condition of formulary placement. The MMA also introduced a new reimbursement methodology based on average sales prices for physician-administered drugs, which is generally believed to have resulted in lower Medicare reimbursement for physician-administered drugs. These cost reduction initiatives and other provisions of this legislation provide additional pressure to contain and reduce drug prices and could decrease the coverage and price that we receive for any approved products and could seriously harm our business. Although the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations when setting their own reimbursement rates, and any reimbursement reduction resulting from the MMA may result in a similar reduction in payments from private payers.

In March 2010, the Patient Protection and Affordable Care Act, or PPACA, which was intended to broaden access to health insurance, constrain and reduce the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms, was passed into law. Effective in October 2010, the PPACA revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, beginning in 2011, the law imposed a significant annual fee on companies that manufacture or import branded prescription drug products. We do not know the full effects that the PPACA will have on our commercialization efforts but we believe it is likely that the law will continue the pressure on pharmaceutical pricing, especially under the Medicare program, and also may increase our regulatory burdens and operating costs. If one or more of our product candidates reaches commercialization, such changes may have a significant impact on our ability to set a price we believe is fair for our products and may adversely affect our ability to generate revenue and achieve or maintain profitability. We expect further federal and state proposals and health care reforms to continue to be proposed by legislators, which could limit the prices that can be charged for the products we develop and may limit our commercial opportunity.

Moreover, in markets outside the US, including Japan, Canada and the countries in the EU, pricing of pharmaceutical products is subject to governmental control. Evaluation criteria used by many EU government agencies for the purposes of pricing and reimbursement typically focus on a product's degree of innovation and its ability to meet a clinical need unfulfilled by currently available therapies. The PPACA created a similar entity, the Patient- Centered Outcomes Research Institute (PCORI) designed to review the effectiveness of treatments and medications in federally-funded health care programs. The PCORI began its first research initiatives recently, and an adverse result may result in a treatment or product being removed from Medicare or Medicare coverage. The decisions of such governmental agencies could affect our ability to sell our products profitably.

Government health care reform could increase our costs, and could adversely affect our revenue and results of operations.

Our industry is highly regulated and changes in law may adversely impact our business, operations or financial results. Substantial new requirements affecting compliance were enacted as part of the PPACA, which may require us to modify our business practices with health care practitioners. For example, drug manufacturers are required to report information on payments or transfers of value to US physicians and teaching hospitals as well as investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties. The reported data is posted in searchable form on a public website. Some state laws also prohibit certain gifts to health care providers, require pharmaceutical companies to report payments to health care professionals, and/or require companies to adopt compliance programs or codes of conduct. In addition, other countries, including France, require the disclosure of certain payments to health care professionals.

The reforms imposed by the PPACA significantly impact the pharmaceutical industry; however, the full effects cannot be known until these provisions are fully implemented and CMS and other federal and state agencies all issue applicable regulations or guidance. Moreover, in the coming years, additional changes could be made to governmental healthcare programs that could significantly impact the success of our products or product candidates. We will continue to evaluate the PPACA, as amended, the implementation of regulations or guidance related to various provisions of the PPACA by federal agencies, as well as trends and changes that may be encouraged by the legislation and that may potentially have an impact on our business over time. The cost of implementing more detailed record keeping systems and otherwise complying with these requirements could substantially increase our costs.

We will need approval from the FDA and other regulatory authorities in jurisdictions outside the US for our proposed trade names. Any failure or delay associated with such approvals may delay the commercialization of our products.

Any trade name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the US Patent and Trademark Office, or PTO. The FDA typically conducts a rigorous review of proposed trade names, including an evaluation of potential for confusion with other trade names and medication error. The FDA also may object to a trade name if it believes the name is inappropriately promotional. The FDA preliminarily approved our use of the name ARIKAYCE as our proposed trade name for our liposomal amikacin for inhalation product candidate. Even after the FDA approves a trade name, the FDA may request that we adopt an alternative name for the product if adverse event reports indicate a potential for confusion with other trade names and medication error. If we are required to adopt an alternative name, the commercialization of ARIKAYCE could be delayed or interrupted, which would limit our ability to commercialize ARIKAYCE and generate revenues. In December 2012, we learned that the EMA had no objection to our request to use the name ARIKAYCE.

If we are found in violation of federal or state "fraud and abuse" laws, we may be required to pay a penalty or may be suspended from participation in federal or state health care programs, which may adversely affect our business, financial condition and results of operations.

In the US, we are subject to various federal and state health care "fraud and abuse" laws, including anti-kickback laws, false claims laws and other laws intended to reduce fraud and abuse in federal and state health care programs. The federal Anti-Kickback Statute makes it illegal for any person, including a prescription drug manufacturer or a party acting on its behalf, to knowingly and willfully solicit, receive, offer or pay any remuneration that is intended to induce the referral of business, including the purchase, order or prescription of a particular drug for which payment may be made under a federal health care program, such as Medicare or Medicaid. Under federal government regulations, some arrangements, known as safe harbors, are deemed not to violate the federal Anti-Kickback Statute. Although we seek to structure our business arrangements in compliance with all applicable requirements, these laws are broadly written, and it is often difficult to determine precisely how the law will be applied in specific circumstances. Accordingly, it is possible that our practices may be challenged under the federal Anti-Kickback Statute. False claims laws prohibit anyone from knowingly and willfully presenting or causing to be presented for payment to third-party payers, including government payers, claims for reimbursed drugs or services that are false or fraudulent, claims for items or services that were not provided as claimed, or claims for medically unnecessary items or services. Cases have been brought under false claims laws alleging that off-label promotion of pharmaceutical products or the provision of kickbacks has caused health care providers to submit false claims to governmental health care programs when they prescribe drugs or fill prescriptions for off-label purposes. Under the Health Insurance Portability and Accountability Act of 1996, we are prohibited from knowingly and willfully executing a scheme to defraud any health care benefit program,

including private payers, or 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 health care benefits, items or services. Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including fines or exclusion or suspension from federal and state health care programs such as Medicare and Medicaid and debarment from contracting with the US government. In addition, private individuals have the ability to bring actions on behalf of the government under the federal False Claims Act as well as under the false claims laws of several states.

Many states have adopted laws similar to the federal anti-kickback statute, some of which apply to the referral of patients for health care services reimbursed by any source, not just governmental payers. In addition, California and a few other states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America, or PhRMA, Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. Health record privacy laws may limit access to information identifying those individuals who may be prospective users or prohibit contact with any persons enrolled in Medicare or Medicaid. There are ambiguities as to what is required to comply with these state requirements, and we could be subject to penalties if a state determines that we have failed to comply with an applicable state law requirement.

Neither the government nor the courts have provided definitive guidance on the application of fraud and abuse laws to our business. Law enforcement authorities are increasingly focused on enforcing these laws, and it is possible that some of our practices may be challenged under these laws. While we believe we have structured our business arrangements to comply with these laws, it is possible that the government could allege violations of, or convict us of violating, these laws. If we are found in violation of one of these laws, we could be required to pay a penalty and could be suspended or excluded from participation in federal or state health care programs, and our business, financial condition and results of operations may be adversely affected.

Risks Related to Our Intellectual Property

If we are unable to protect our intellectual property rights adequately, the value of our product candidates could be diminished.

Our success will depend in part on our ability to protect proprietary technology and to obtain patent protection for our products, prevent third parties from infringing on our patents and refrain from infringing on the patents of others, both domestically and internationally.

In addition, the patent situation in the field of biotechnology and pharmaceuticals generally is highly uncertain and involves complex legal, technical, scientific and factual questions. We intend to actively pursue patent protection for products resulting from our research and development activities that have significant potential commercial value. We may not be able to obtain additional issued patents relating to our technology or products.

Even if issued, patents issued to us or our licensors may be challenged, narrowed, invalidated, held to be unenforceable or circumvented, which could limit our ability to stop competitors from marketing similar products or reduce the term of patent protection we may have for our products. We cannot assure you that any patents obtained will afford us adequate protection or provide us with any meaningful competitive advantages against these competitors.

US patents and patent applications may also be subject to interference or derivation proceedings, and US patents may be subject to re-examination proceedings, reissue, post-grant review and/or inter partes review in the USPTO. Foreign patents may be subject to opposition or comparable proceedings in the corresponding foreign patent office, which could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such interference, derivation, re-examination, post-grant review, inter partes review and opposition proceedings may be costly.

Changes in either patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. For example, the America Invents Act was signed into law in the United States in September 2011, with phased implementation through March 2013, and includes a number of changes to established practices. These include the transition to a first-inventor-to-file system, establishment of new procedures for challenging patents and implementation of different methods for invalidating patents. We cannot predict the impact that new laws, government rule-making, implementing regulations and applicable case law may have on the strength of our patents. Certain reforms may make it easier for competitors to challenge our patents and could have a material adverse effect on our business and prospects. In addition, any patents we procure may require cooperation with companies holding related patents and we may have difficulty forming a successful relationship with such other companies.

If we are not able to adequately prevent disclosure of trade secrets and other proprietary information, the value of our product candidates could be significantly diminished.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, advisors, collaborators, and other third parties and partners to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information or may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, third parties may independently develop or discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative is considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time whether and how the FDA's disclosure policies may change in the future. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and any failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

We may not be able to enforce our intellectual property rights throughout the world.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to life sciences. This could make it difficult for us to stop the infringement of our patents or in-licensed patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner may be required to grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit.

Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business. Our efforts to protect our intellectual property rights in such countries may be inadequate. In addition, changes in the law and legal decisions by courts in the United States and foreign countries may affect our ability to obtain adequate protection for our technology and to enforce intellectual property rights.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information.

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our corporate partners, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover trade secrets and proprietary information. Costly and time- consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our ability to successfully compete in the industry.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts, prevent us from commercializing our products or increase the costs of commercializing our products.

Third parties may claim that we have infringed upon or misappropriated their proprietary rights. Third parties may attempt to obtain patent protection relating to the production and use of our product candidates. We cannot assure you that any existing third-party patents, or patents that may later issue to third parties, would not negatively affect our commercialization of ARIKAYCE, INS1009 or any other product. We cannot assure you that such patents can be avoided or invalidated or would be licensed to us at commercially reasonable rates or at all. We cannot assure you that we will be successful in any intellectual property litigation that may arise or that such litigation would not have an adverse effect on our business, financial condition, results of operation or prospects. In the event of a successful claim against us for infringement or misappropriation of a third party's proprietary rights, we may be required to take actions including but not limited to the following:

- Pay damages, including up to treble damages, and the other party's attorneys' fees, which may be substantial;
- Cease the development, manufacture, marketing and sale of products or use of processes that infringe the proprietary rights of others;
- Expend significant resources to redesign our products or our processes so that they do not infringe the proprietary rights of others, which may not be possible;
- Redesign our products or processes to avoid third-party proprietary rights, which means we may suffer significant regulatory delays associated with conducting additional clinical trials or other steps to obtain regulatory approval; and/or
- Obtain one or more licenses arising out of a settlement of litigation or otherwise from third parties which license(s) may not be available to us on acceptable terms or at all.

Furthermore, litigation with any third party, even if the allegations are without merit, would likely be expensive and time-consuming and divert management's attention.

In particular, PAH is a competitive indication with established products, including other formulations of treprostinil. Our supply of the active pharmaceutical ingredient for INS1009 is dependent upon a single supplier. The supplier owns patents on its manufacturing process and we have filed patent applications for INS1009. A competitor in the PAH indication may claim that we or our

supplier have infringed upon or misappropriated their proprietary rights. We cannot be sure that we or our supplier will be successful in any intellectual property litigation that may arise or that such litigation would not have an adverse effect on our business, financial condition, results of operation or prospects.

Any lawsuits relating to infringement of intellectual property rights necessary to defend ourselves or enforce our rights may be costly and time consuming.

Any conclusions we may have reached regarding non-infringement, inapplicability or invalidity of a third party's intellectual property are based in significant part on a review of publicly available databases and other information. There may be information not available to us or otherwise not reviewed by us that could change our conclusions. Moreover, the scope and validity of patent claims depend significantly on facts and circumstances, and a court's conclusions as to these matters may differ from the conclusions that we have reached.

We may have to undertake costly litigation to enforce any patents issued or licensed to us or to confirm the scope and validity of another party's proprietary rights. We cannot assure you that a court would not invalidate our issued or licensed intellectual property. An adverse outcome in litigation or interference or other proceeding in any court or patent office could materially adversely affect our ability to develop and commercialize our product candidates.

If we fail to comply with our obligations in our license agreements for our product candidates, we could lose license rights that are important to our business.

We currently have a licensing agreement with PARI for use of the optimized eFlow Nebulizer System for delivery of ARIKAYCE in treating patients with NTM infections. We have rights to several US and foreign issued patents, and patent applications involving improvements to the optimized eFlow Nebulizer System. Under the licensing agreement, PARI is entitled to receive payments either in cash, qualified stock or a combination of both, at PARI's discretion, based on achievement of certain milestone events including phase 3 trial initiation, first acceptance of MAA submission (or equivalent) in the US of ARIKAYCE and the device, first receipt of marketing approval in the US for ARIKAYCE and the device, and first receipt of marketing approval in a major EU country for ARIKAYCE and the device. There can be no assurance that the foregoing milestone events will be achieved and therefore there can be no assurance that we will make any future payments. We have certain obligations under this licensing agreement in relation to specified licensed indications. With respect to CF, we are obligated to use commercially reasonable efforts to develop, obtain regulatory and reimbursement approval, market and sell ARIKAYCE in two or more major European countries. With respect to NTM, CF and bronchiectasis, we have specific obligations to use commercially reasonable efforts to achieve certain developmental and regulatory milestones by set deadlines. Additionally, for NTM, we are obligated to use commercially reasonable efforts to achieve certain commercial milestones in the US, Europe and Canada. The consequences of our failing to use commercially reasonable efforts to achieve certain commercial milestones are context-specific, but include ending PARI's non-compete obligation, making the license non-exclusive and terminating the license, in each case with respect to the applicable indication. Termination of the licensing agreement or loss of exclusive rights may occur if we fail to meet our obligations, including payment of royalties to PARI, or if we do not meet certain milestones contained in the licensing agreement such as obtaining marketing approval or achieving the first commercial sale of ARIKAYCE.

Risks Related to Our Industry

We operate in a highly competitive and changing environment, and if we are unable to adapt to our environment, we may be unable to compete successfully.

Biotechnology and related pharmaceutical technology have undergone and are likely to continue to experience rapid and significant change. We expect that the technologies associated with biotechnology research and development will continue to develop rapidly. Our future success will depend in large part on our ability to maintain a competitive position with respect to these technologies and to obtain and maintain protection for our intellectual property. Any compounds, products or processes that we develop may become obsolete before we recover any expenses incurred in connection with their development. Rapid technological change could make our products obsolete, and materially adversely affect our business, financial condition, results of operations or prospects.

We expect that successful competition will depend, among other things, on product efficacy, safety, reliability, availability, timing and scope of regulatory approval and price. Specifically, we expect crucial factors will include the relative speed with which we can develop products, complete the clinical testing and regulatory approval processes and supply commercial quantities of the product to the market. We expect competition to increase as technological advances are made and commercial applications broaden.

In each of our potential product areas, we face substantial competition from pharmaceutical, biotechnology and other companies, universities and research institutions. Relative to us, most of these entities have substantially greater capital resources, research and development staffs, facilities and experience in conducting clinical studies and obtaining regulatory approvals, as well as in manufacturing and marketing pharmaceutical products. Many of our competitors may achieve product commercialization or patent protection earlier than us. Furthermore, we believe that our competitors have used, and may continue to use, litigation to gain a competitive advantage. Finally, our competitors may use different technologies or approaches to the development of products similar to the products we are seeking to develop. We cannot assure you that if ARIKAYCE is approved for NTM that it will be able to compete successfully in the marketplace.

Competitors could develop and obtain FDA or other regulatory approval of products containing amikacin, which could adversely affect our competitive position in all ARIKAYCE-related indications.

In the event there are other amikacin products approved by the FDA or other regulatory agencies for any use, physicians may elect to prescribe those products rather than ARIKAYCE to treat the indications for which ARIKAYCE may receive approval, which is commonly referred to as off-label use. Although regulations prohibit a drug company from promoting off-label use of its product, the FDA and other regulatory agencies do not regulate the practice of medicine and as a result cannot direct physicians as to what product to prescribe to their patients. As a result, we would have limited ability to prevent any off-label use of a competitor's product to treat diseases for which we have received FDA or other regulatory agency approval, even if such use violates our patents or orphan drug exclusivity for the use of amikacin to treat such diseases. This could negatively affect our results of operations or business.

Competitors could develop and obtain FDA or other regulatory approval of antibiotic products that are more effective, safer, tolerable or more convenient or less expensive than our products in development or existing products, which could adversely affect our competitive position in all ARIKAYCE-related indications.

There are potential competitive products, both approved and in development, which include oral, systemic, or inhaled antibiotic products to treat chronic respiratory infections. If any of our competitors develops a product that is more effective, safer, tolerable or, convenient or less expensive than ARIKAYCE, it would adversely affect our ability to generate revenues. We also may face lower priced generic competitors if third-party payers encourage use of generic or lower-priced versions of our product or if competing products are imported into the US or other countries where we may sell ARIKAYCE.

If another party obtains orphan drug exclusivity for a product that is essentially the same as a product we are developing for a particular indication, we may be precluded or delayed from commercializing the product in that indication.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition. See "Business—Government Regulation—Orphan Drugs—United States." The company that obtains the first marketing approval from the FDA for a designated orphan drug for a rare disease receives marketing exclusivity for use of that drug for the designated condition for a period of seven years. Similar laws exist in EU with a term of ten years. See "Business—Government Regulation—Orphan Drugs—Europe." If a competitor obtains approval of the same drug for the same indication or disease before us, we would be prohibited from obtaining approval for our product for seven or more years, unless our product can be shown to be clinically superior. In addition, more than one drug may be approved by the FDA for the same orphan indication or disease as long as the drugs are different drugs. As a result, even if one of our products is approved and receives orphan drug exclusivity, the FDA may approve different drugs for use in treating the same indication or disease covered by our product, which could adversely affect our competitive position.

If we obtain orphan exclusivity for a product, the FDA may approve another product during our orphan exclusivity period for the same indication under certain circumstances.

The Orphan Drug Act was created to encourage companies to develop therapies for rare diseases by providing incentives for drug development and commercialization. One of the incentives provided by the act is seven years of market exclusivity in the United States for the first product in a class licensed for the treatment of a rare disease. Orphan exclusivity will not, however, bar approval of another product under certain circumstances. One such circumstance is if a product with the same active ingredient is proven safe and effective for a different indication. Another circumstance is if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care. FDA may also approve another product with the same active ingredient and the same indication if the company with orphan drug exclusivity is not able to meet market demand. Further, FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. As a result, even if one of our product candidates receives orphan exclusivity, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease. All of the above circumstances could create a more competitive market for us.

Our research, development and manufacturing activities used in the production of ARIKAYCE involve the use of hazardous materials, which could expose us to damages and materially adversely affect our results of operations and financial condition.

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 research and development program and manufacturing activities for ARIKAYCE involve the controlled use of hazardous materials and chemicals. We generally contract with third parties for the disposal of these materials and wastes. Although we believe we are in compliance with all pertinent regulations, we cannot eliminate the risk of environmental contamination, damage to facilities or injury to personnel from the accidental or improper use or control of these materials. In addition to any liability we could have for any misuse by us of hazardous materials and chemicals, we could also potentially be liable for activities of our contract manufacturers or other third parties. Any such liability, or even claims of such liability, could materially adversely affect our results of operations and financial condition. We also could incur significant costs associated with civil or criminal fines and penalties.

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. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We may be subject to product liability claims, and we have only limited product liability insurance.

The manufacture and sale of human therapeutic products involve an inherent risk of product liability claims and associated adverse publicity. We currently have only limited product liability insurance for our products. We do not know if we will be able to maintain existing or obtain additional product liability insurance on acceptable terms or with adequate coverage against potential liabilities. This type of insurance is expensive and may not be available on acceptable terms. If we are unable to obtain or maintain sufficient insurance coverage on reasonable terms or to otherwise protect against potential product liability claims, we may be unable to commercialize our products. A successful product liability claim brought against us in excess of our insurance coverage, if any, may require us to pay substantial amounts and may materially adversely affect our business, financial condition, results of operations or prospects.

Risks Related to Employee Matters and Managing Growth

We are dependent upon retaining and attracting key personnel, the loss of whose services could materially adversely affect our business, financial condition, results of operations and prospects.

We depend highly on the principal members of our scientific and management personnel, the loss of whose services might significantly delay or prevent the achievement of our research, development or business objectives. Our success depends, in large part, on our ability to attract and retain qualified management, scientific and medical personnel, and on our ability to develop and maintain important relationships with commercial partners, leading research institutions and key distributors. We will need to hire additional personnel in anticipation of seeking regulatory approval for and commercial launch of ARIKAYCE.

Competition for skilled personnel in our industry and market is very intense because of the numerous pharmaceutical and biotechnology companies that seek similar personnel. These companies may have greater financial and other resources, offer a greater opportunity for career advancement and

have a longer history in the industry than we do. We also experience competition for the hiring of our scientific and clinical personnel from universities, research institutions, and other third parties. We cannot assure that we will attract and retain such persons or maintain such relationships.

Our inability to retain and attract qualified employees would harm our business.

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

We expect that our potential expansion into areas and activities requiring additional expertise, such as further clinical trials, governmental approvals, manufacturing, sales, marketing and distribution will place additional requirements on our management, operational and financial resources. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees.

The anticipated commercialization of ARIKAYCE and the development of additional product candidates will require significant expenditures by us and place a strain on our resources. If our management is unable to effectively manage our activities in anticipation of commercialization, as well as our development efforts, we may incur higher than expected expenditures or other expenses and our business may otherwise be adversely affected.

Risks Related to our Common Stock and Listing on the Nasdaq Global Select Market

The market price of our stock has been and may continue to be highly volatile.

Our common stock is listed on the Nasdaq Global Select Market under the ticker symbol INSM. The market price of our stock has been and may continue to be highly volatile, and could be subject to wide fluctuations in price in response to various factors, many of which are beyond our control. These factors may include:

- Our listing status on the Nasdaq Global Select Market;
- Results of our clinical studies and preclinical studies, or those of our corporate partners or our competitors;
- Delays in timing of pre-clinical, clinical development and regulatory filings and delays regarding our inability to obtain potential approvals;
- Strategic business decisions;
- Developments in our relationships with corporate partners;
- Developments affecting our corporate partners;
- Negative regulatory action or regulatory approval with respect to our announcement or our competitors' announcements of new products;
- Government regulation, reimbursement changes and governmental investigation or audits related to us or to our products;
- Developments related to our patents or other proprietary rights or those of our competitors;
- Other competitive developments;
- Reports issued by and changes in the position of securities analysts with respect to our stock or changes in stock ownership by investors;

- Operating results below the expectations of securities analysts and investors; and
- The need or perceived need to raise additional capital.

In addition, the stock market has from time to time experienced extreme price and volume fluctuations, which have particularly affected the market prices for emerging biotechnology and pharmaceutical companies like us, and which have often been unrelated to their operating performance. These broad market fluctuations may adversely affect the market price of our common stock.

Historically, when the market price of a stock has been volatile, shareholders are more likely to institute securities and derivative class action litigation against the issuer of such stock. If any of our shareholders were to institute a lawsuit against us, we could incur substantial costs defending the lawsuit. Any lawsuit could divert the time and attention of our management.

Future sales of substantial amounts of common stock in the public market, or the possibility of such sales occurring, could also adversely affect prevailing market prices for our common stock or our future ability to raise capital through an offering of equity securities.

The sale of a significant number of shares of our common stock in the public market could harm the market price of our common stock. The market price for our common stock could also decline, perhaps significantly, as a result of issuances of a large number of shares of our common stock in the public market or even the perception that such issuances could occur.

If we fail to meet the continued listing requirements of the Nasdaq Global Select Market, our common stock may be delisted from the Nasdaq Global Select Market, which may cause the value of an investment in our common stock to decrease.

If a delisting from the Nasdaq Global Select Market were to occur, our common stock may be eligible, upon the application of a market maker, to trade on the OTC Bulletin Board or in the "pink sheets." These alternative markets are generally considered to be less efficient than, and not as broad as, the Nasdaq Global Select Market. Therefore, delisting of our common stock from the Nasdaq Global Select Market could adversely affect the trading price of our common stock and could limit the liquidity of our common stock and therefore could cause the value of an investment in our common stock to decrease.

The ownership interest of existing shareholders will be diluted by the exercise of options issued by us or to the extent that we issue additional common stock in connection with any offerings of securities, strategic transactions, or otherwise.

As of December 31, 2015, 5.3 million shares of our common stock are potentially issuable under outstanding restricted stock units and stock options to our employees, officers, directors and consultants.

The conversion or exercise of some or all of our restricted stock units and options will dilute the ownership interests of existing shareholders. Any sales in the public market of the common stock issuable upon such conversion or exercise could adversely affect prevailing market prices of our common stock.

Additionally, our Articles of Incorporation currently authorize us to issue up to 500 million common shares. As of December 31, 2015 we had 61.8 million shares of common stock outstanding. To the extent that we issue additional common stock in connection with any offerings of securities,

strategic transactions, or otherwise, the ownership interest of existing shareholders will be further diluted.

Historically we have not paid dividends on our common stock, and we have no plans to pay dividends in the foreseeable future.

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so for the foreseeable future. We currently anticipate that we will retain any future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased their shares.

Certain provisions of Virginia law and our articles of incorporation and amended and restated bylaws could hamper a third party's acquisition of, or discourage a third party from attempting to acquire control of us.

Certain provisions of Virginia law and our articles of incorporation and amended and restated bylaws could hamper a third party's acquisition of, or discourage a third party from attempting to acquire control of us or limit the price that investors might be willing to pay for shares of our common stock. These provisions include:

- A provision allowing us to issue preferred stock with rights senior to those of the common stock without any further vote or action by the holders of the common stock. The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to the holders of common stock or could adversely affect the rights and powers, including voting rights, of the holders of the common stock. In certain circumstances, such issuance could have the effect of decreasing the market price of the common stock;
- The existence of a staggered board of directors in which there are three classes of directors serving staggered three-year terms, thus expanding the time required to change the composition of a majority of directors and perhaps discouraging someone from making an acquisition proposal for us;
- Our amended and restated bylaws' requirement that shareholders provide advance notice when nominating director candidates to serve on our Board of Directors;
- The inability of shareholders to convene a shareholders' meeting without the chairman of the board, the president or a majority of the board of directors first calling the meeting; and
- The application of Virginia law prohibiting us from entering into a business combination with the beneficial owner of 10% or more of our outstanding voting stock for a period of three years after the 10% or greater owner first reached that level of stock ownership, unless we meet certain criteria.

In addition, we previously had a "poison pill" shareholder rights plan, which expired in May 2011. Under Virginia law, our Board of Directors may implement a new shareholders rights plan without shareholder approval. Our Board of Directors intends to regularly consider this matter, even in the absence of specific circumstances or takeover proposals, to facilitate its future ability to quickly and effectively protect shareholder value.

Other Risks Related to our Business

Corporate governance and public disclosure requirements add uncertainty to our compliance policies and increase our costs of compliance.

Changing laws, regulations and standards relating to accounting, corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, other SEC regulations, and the Nasdaq Global Select Market rules, are creating uncertainty for companies like ours. These laws, regulations and standards may lack specificity and are subject to varying interpretations. Their application in practice may evolve over time, as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs of compliance as a result of ongoing revisions to such corporate governance standards.

In particular, our efforts to comply with Section 404 of the Sarbanes-Oxley Act of 2002, to furnish a report by management on, among other things, the effectiveness and the related regulations regarding our required assessment of our internal controls over financial reporting and our external auditors' audit of our internal control over financial reporting requires the commitment of significant financial and managerial resources. We consistently assess the adequacy of our internal controls over financial reporting, remediate any control deficiencies that may be identified, and validate through testing that our controls are functioning as documented. While we do not anticipate any material weaknesses, the inability of management and our independent auditor to provide us with an unqualified report as to the effectiveness of our internal controls over financial reporting for future year ends could result in adverse consequences to us, including, but not limited to, a loss of investor confidence in the reliability of our financial statements, which could cause the market price of our stock to decline. For example, in connection with our review of internal control over financial reporting as of December 31, 2012, we determined that we did not adequately implement certain controls over the administration, accounting and oversight of our 2000 Stock Incentive Plan, and we concluded that a material weakness in our internal control over financial reporting existed as of December 31, 2012. The existence of this or one or more other material weaknesses or significant deficiencies in our internal control over financial reporting could result in errors in our financial statements, and substantial costs and resources may be required to rectify any internal control deficiencies. Any material weaknesses may materially adversely affect our ability to report accurately our financial condition and results of operations in a timely and reliable manner. In addition, although we continually review and evaluate internal control systems to allow management to report on the sufficiency of our internal controls, we cannot assure you that we will not discover weaknesses in our internal control over financial reporting. Any such weakness or failure to remediate a material weakness could materially adversely affect our ability to comply with applicable financial reporting requirements and the requirements of our various agreements.

We are committed to maintaining high standards of corporate governance and public disclosure, and our efforts to comply with evolving laws, regulations and standards in this regard have resulted in, and are likely to continue to result in, increased general and administrative expenses and a diversion of management time and attention from revenue-generating activities to compliance activities. In addition, the laws, regulations and standards regarding corporate governance may make it more difficult for us to obtain director and officer liability insurance. Further, our board members, chief executive officer and chief financial officer could face an increased risk of personal liability in connection with their performance of duties. As a result, we may face difficulties attracting and retaining qualified board members and executive officers, which could harm our business. If we fail to comply with new or changed laws, regulations or standards of corporate governance, our business and reputation may be harmed.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our business operations, including our drug development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other 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 adverse effect on our business operations, including a material disruption of our drug development programs. Unauthorized disclosure of sensitive or confidential client or employee data, whether through breach of computer systems, systems failure, employee negligence, fraud or misappropriation, or otherwise, could damage our reputation. Similarly, unauthorized access to or through our information systems and networks, whether by our employees or third parties, could result in negative publicity, legal liability and damage to our reputation. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of our drug candidates 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 was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our drug candidates could be delayed.

Although we have general liability insurance coverage, including coverage for errors or omissions, there can be no assurance that our coverage will cover all claims, continue to be available on reasonable terms or will be sufficient in amount to cover one or more large claims, or that the insurer will not disclaim coverage as to any future claim. The successful assertion of one or more large claims against us that exceed or are not covered by our insurance coverage or changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could have a material adverse effect on our business, results of operations and financial condition.

We are subject to the U.S. Foreign Corrupt Practices Act and other anti-corruption laws or trade control laws, as well as other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures, and legal expenses, which could adversely affect our business, financial condition and results of operations.

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act (the "FCPA") and other anti-corruption laws that apply in countries where we do business. The FCPA, UK Bribery Act and these other laws generally prohibit us, our employees and our intermediaries making prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We operate in jurisdictions that pose a risk of potential FCPA violations, and we participate in joint ventures and relationships with third parties whose actions could potentially subject us to liability under the FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the U.S. Department of Commerce's Bureau of Industry and Security, the U.S. Department of Treasury's Office of Foreign Asset Control, and various non-U.S. government entities, including applicable export control regulations, economic sanctions on countries and persons, customs requirements, currency exchange regulations and transfer pricing regulations (collectively, the "Trade Control laws").

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anticorruption laws, including the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the FCPA other anti- corruption laws or Trade Control laws by U.S. or foreign authorities could also have an adverse impact on our reputation, business, financial condition and results of operations.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We currently lease 56,617 square feet of laboratory and office space in Bridgewater, New Jersey. The initial term of the lease will expire in November 2019, and we have the option to extend the lease for two additional five year periods beyond the initial term. In 2016, we leased office space in Ireland and the Netherlands.

We also lease approximately 19,000 square feet of office space in Richmond, Virginia. The lease expires in October 2016. Our corporate headquarters were formerly located in Richmond but we closed this facility. In November 2014, we entered into an agreement to sublet this space for the remainder of the lease term.

ITEM 3. LEGAL PROCEEDINGS

From time to time, we are a party to various lawsuits, claims and other legal proceedings that arise in the ordinary course of our business. While the outcomes of these matters are uncertain, management does not expect that the ultimate costs to resolve these matters will have a material adverse effect on our consolidated financial position, results of operations or cash flows. See Note 11 to the Notes to the Consolidated Financial Statements included in this report for a description of our current legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

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

Our trading symbol is "INSM." Our common stock currently trades on the Nasdaq Global Select Market. Until February 3, 2014, our common stock traded on the Nasdaq Capital Market. The following table lists the high and low sale prices per share for our common stock on a quarterly basis for both 2015 and 2014.

Fiscal Year 2015	High	Low
Fourth Quarter	$ 21.14	$ 15.31
Third Quarter	$ 28.66	$ 17.07
Second Quarter	$ 25.39	$ 19.87
First Quarter	$ 22.59	$ 13.93

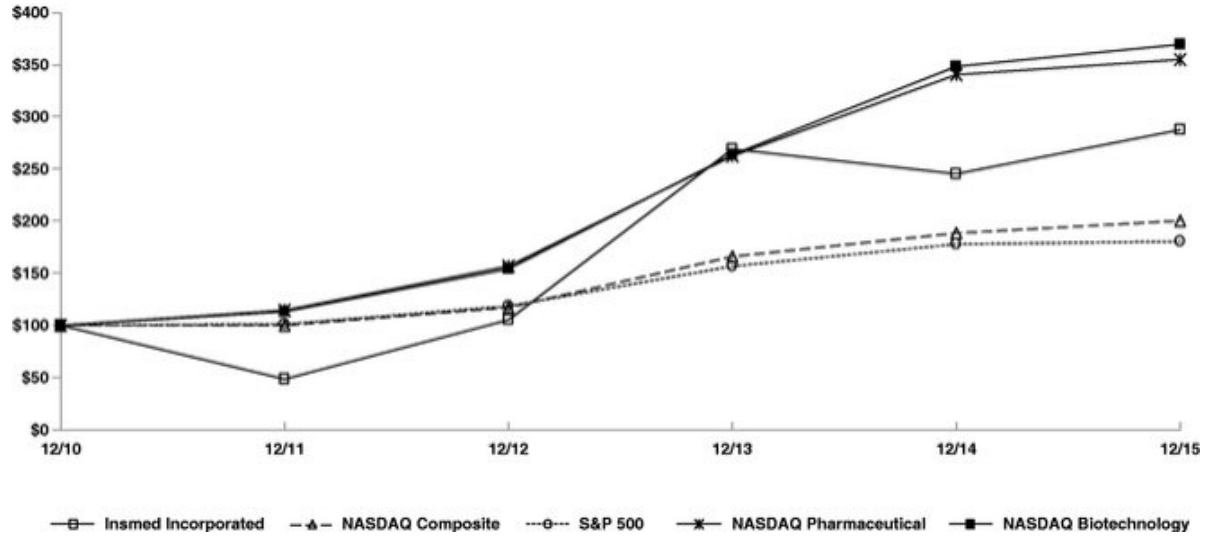
Fiscal Year 2014	High	Low
Fourth Quarter	$ 16.42	$ 12.57
Third Quarter	$ 20.11	$ 11.65
Second Quarter	$ 19.98	$ 12.10
First Quarter	$ 21.54	$ 15.91

On February 1, 2016, the last reported sale price for our common stock on the Nasdaq Global Select Market was $13.54 per share. As of February 1, 2016, there were 141 holders of record of our common stock.

On December 15, 2014, we entered into a Stock Purchase Agreement with Hercules pursuant to which we issued 70,771 shares of our common stock, par value $0.01 per share (which represented less than 1% of the outstanding Common Stock as of the date thereof), at a price of $14.13 per share (the closing price on December 12, 2014), for an aggregate purchase price of approximately $1.0 million. The securities sold in the private placement were not registered under the Securities Act of 1933, as amended (the "Act") and may not be offered or sold in the United States in the absence of an effective registration statement or exemption from the registration requirements under the Act. We believe that the issuance of the securities in this transaction was exempt from registration under Section 4(2) of the Act.

We have never declared or paid cash dividends on our common stock. We anticipate that we will retain all earnings, if any, to support operations and to finance the growth and development of our business for the foreseeable future. Under the terms of our loan agreement with Hercules, we are prohibited from declaring or paying any cash dividend or making a cash distribution on any class of our stock or on other equity interest, except that our subsidiaries (defined in the Loan Agreement as a corporate entity in which we control more than 50% of the voting securities) may pay dividends or make distributions to their equity owners. Any future determination as to the payment of dividends will be dependent upon these and any contractual or other restrictions to which we may be subject and, to the extent permissible thereunder, will be at the sole discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors our board of directors deems relevant.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*
Among Insmed Incorporated, the NASDAQ Composite Index, the S&P 500 Index,
the NASDAQ Pharmaceutical Index, and the NASDAQ Biotechnology Index



* $100 invested on 12/31/10 in stock or index, including reinvestment of dividends.
Fiscal year ending December 31.

ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data reflects our consolidated statements of operations and consolidated balance sheets as of and for the years ended December 31, 2015, 2014, 2013, 2012 and 2011. The data below should be read in conjunction with, and is qualified by reference to, "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our

consolidated financial statements and notes thereto contained elsewhere in this Annual Report on Form 10-K.

	Year Ended December 31,				
	2015	2014	2013	2012	2011 (1)
	(in thousands, except per share data)				
Historical Statement of Operations Data:					
Revenues	$ -	$ -	$ 11,500	$ -	$ 4,417
Operating expenses:					
Research and development	74,277	56,292	44,279	29,781	28,623
General and administrative	43,216	31,073	22,236	12,657	11,523
Impairment loss	-	-	-	-	25,990
Total operating expenses	117,493	87,365	66,515	42,438	66,136
Operating loss	(117,493)	(87,365)	(55,015)	(42,438)	(61,719)
Investment income	261	58	166	1,822	2,064
Interest expense	(2,889)	(2,415)	(2,412)	(763)	(10)
Other, net	(33)	141	(33)	5	1
Loss before income taxes	(120,154)	(89,581)	(57,294)	(41,374)	(59,664)
Income tax benefit	(1,971)	(10,422)	(1,221)	-	-
Net loss	(118,183)	(79,159)	(56,073)	(41,374)	(59,664)
Accretion of beneficial conversion feature	-	-	-	-	(9,175)
Net loss attributable to common stockholders	$ (118,183)	$ (79,159)	$ (56,073)	$ (41,374)	$ (68,839)
Basic and diluted net loss attributable to common stockholders per share	$ (2.02)	$ (1.84)	$ (1.60)	$ (1.56)	$ (2.95)
Weighted average basic and diluted common shares outstanding	58,633	43,095	34,980	26,545	23,348
Historical Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 282,876	$ 159,226	$ 113,894	$ 90,782	$ 76,272
Certificate of deposit	$ -	$ -	$ -	$ 2,153	$ 2,085
Total assets	$ 356,556	$ 230,864	$ 176,498	$ 153,561	$ 139,833
Current portion of long-term debt	$ 3,113	$ -	$ 3,283	$ 3,007	$ -
Long-term debt, net of current portion	$ 22,027	$ 24,856	$ 16,338	$ 16,221	$ -
Stockholders' equity	$ 311,698	$ 186,237	$ 143,324	$ 120,882	$ 134,267

(1) During the first quarter of 2011, our board of directors authorized a one-for-ten reverse stock split. All share and per share amounts included in the above selected financial data give retroactive effect to the one-for-ten stock split for all periods presented.

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

The following discussion also should be read in conjunction with our consolidated financial statements and the notes thereto.

OVERVIEW

Insmed is a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. Our lead product candidate is ARIKAYCE™, or liposomal amikacin for inhalation (LAI), which is in late-stage development for patients with nontuberculous mycobacteria (NTM) lung disease, a rare and often chronic infection that is capable of causing irreversible lung damage and can be fatal. Our earlier stage pipeline includes INS1009, a nebulized prodrug formulation of treprostinil, a vasodilator of pulmonary arterial vascular beds. We believe INS1009 may offer a differentiated product profile with therapeutic potential in pulmonary arterial hypertension (PAH), idiopathic pulmonary fibrosis (IPF), sarcoidosis, and severe refractory asthma.

We are conducting a global phase 3 clinical study of ARIKAYCE (the 212 or CONVERT study) in adult patients with NTM lung disease caused by *Mycobacterium avium* complex (MAC), the predominant infective species in NTM lung disease in the United States (US), Europe, and Japan. The European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) is reviewing our marketing authorization application (MAA) seeking approval of ARIKAYCE for the treatment of MAC lung disease in adult patients who have persistent positive sputum cultures despite the use of medically appropriate first-line therapy. We are also advancing a phase 1 study of INS1009 in healthy subjects. In addition to INS1009, our earlier-stage pipeline includes a number of preclinical compounds that we are evaluating in multiple rare diseases of unmet medical need, including methicillin-resistant staph aureus (MRSA), NTM, PAH, and sarcoidosis. We are also evaluating additional formulations and delivery options for treprostinil, including delivery via a metered dose inhaler. To complement our internal research, we actively seek in-licensing and acquisition opportunities for a broad range of rare diseases.

We were incorporated in the Commonwealth of Virginia on November 29, 1999. On December 1, 2010, we completed a business combination with Transave, Inc., a privately held, New Jersey-based pharmaceutical company focused on the development of differentiated and innovative inhaled pharmaceuticals for the site-specific treatment of serious lung infections. Our continuing operations are based on the technology and products historically developed by Transave. During 2015 we formed subsidiaries in a number of countries in Europe in preparation for the commercialization of ARIKAYCE, upon approval in the European Union, and to support our global tax structure. The Company has operations in the US, Ireland, Germany, France, the United Kingdom (UK) and the Netherlands. Our principal executive offices are located at 10 Finderne Avenue, Building 10, Bridgewater, New Jersey 08807 and our phone number is (908) 977-9900. Our Company website is www.insmed.com. The information presented in our website is not a part of this Annual Report and the reference to our website is intended to be an inactive textual reference only.

KEY COMPONENTS OF OUR STATEMENT OF OPERATIONS

Revenues

In 2015, the French National Agency for Medicines and Health Products Safety (ANSM) granted LAI a Temporary Authorization for Use (Autorisation Temporaire d'Utilisation or ATU). Pursuant to this program, we shipped ARIKAYCE to pharmacies after receiving requests from physicians for patients in France. For the year ended December 31, 2015, the revenue recorded from

the ATU program was immaterial to disclose and is included in "other income." We are initiating expanded access programs (EAPs) in other select territories in Europe, some of which may be fully reimbursed. EAPs are intended to make products available before they are commercially available in accordance with local regulations. We did not recognize any revenue in 2014. In 2013, our other revenue solely consisted of an $11.5 million payment received from Premacure Holdings AB and Premacure AB of Sweden (now Shire plc) in exchange for the Company's right to receive royalties under its license agreement with Premacure. We recorded this as other revenue after all four revenue recognition criteria were present and we had no continuing performance obligations related to the payment received. Besides the ATU revenue in France, we currently do not recognize any revenue from product sales or other sources.

Research and Development Expenses

Research and development expenses consist primarily of salaries, benefits and other related costs, including stock-based compensation, for personnel serving in our research and development functions. Expenses also include other internal operating expenses, the cost of manufacturing our drug candidate for clinical study, the cost of conducting clinical studies, and the cost of conducting preclinical and research activities. Our expenses related to manufacturing our drug candidate for clinical study are primarily related to activities at contract manufacturing organizations that manufacture ARIKAYCE for our use. Our expenses related to clinical trials are primarily related to activities at contract research organizations that conduct and manage clinical trials on our behalf. These contracts set forth the scope of work to be completed at a fixed fee or amount per patient enrolled. Payments under these contracts primarily depend on performance criteria such as the successful enrollment of patients or the completion of clinical trial milestones as well as time-based fees. Expenses are accrued based on contracted amounts applied to the level of patient enrollment and to activity according to the clinical trial protocol. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are then recognized as an expense as the related goods are delivered or the services are performed, or when the goods or services are no longer expected to be provided.

Since 2011, we have focused our development activities principally on our proprietary, advanced liposomal technology designed specifically for inhalation lung delivery. In 2013, we completed a phase 3 trial in Europe and Canada in which we evaluated ARIKAYCE in CF patients with *Pseudomonas* lung infections. In 2014, we completed a phase 2 clinical trial in the US and Canada of ARIKAYCE in patients with NTM lung infections. In 2015, we commenced a global phase 3 trial for ARIKAYCE for patients with NTM lung infections. Since our business combination with Transave, the majority of our research and development expenses have been for our ARIKAYCE program. Our development efforts in 2015 principally relate to the development of ARIKAYCE in the NTM indication and, to a lesser extent, for INS1009.

Our clinical trials are subject to numerous risks and uncertainties that are outside of our control, including the possibility that necessary regulatory approvals may not be obtained. In addition, the duration and the cost of clinical trials may vary significantly from trial to trial over the life of a project as a result of differences in the study protocol for each trial as well as differences arising during the clinical trial, including, among others, the following:

- The number of patients that ultimately participate in the trial;
- The duration of patient follow-up that is determined to be appropriate in view of results;
- The number of clinical sites included in the trials;
- The length of time required to enroll suitable patient subjects; and
- The efficacy and safety profile of the product candidate.

Our clinical trials may be subject to delays, particularly if we are unable to produce clinical trial material in sufficient quantities and of sufficient quality to meet the schedule for our clinical trials. Moreover, all of our product candidates must overcome significant regulatory, technological, manufacturing and marketing challenges before they can be successfully commercialized. Any significant delays that occur or additional expenses that we incur may have a material adverse effect on our financial position and may require us to raise additional capital sooner or in larger amounts than is presently expected. In addition, as a result of the risks and uncertainties related to the development and approval of our product candidates and the additional uncertainties related to our ability to market and sell these products once approved for commercial sale, we are unable to provide a meaningful prediction regarding when, if at all, we will generate positive cash inflow from these projects.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits and other related costs, including stock-based compensation, for personnel serving in our executive, finance and accounting, legal, pre-commercial, corporate development, information technology, program management and human resource functions. General and administrative expenses also include professional fees for legal, including patent-related expenses, consulting, insurance, board of director fees, tax and accounting services. We expect that our general and administrative expenses will increase in order to support increased levels of development activities and commencement of commercialization activities for our product candidates, specifically in Europe.

Debt Issuance Costs

Debt issuance costs are amortized to interest expense using the effective interest rate method over the term of the debt. Our balance sheet reflects debt net of debt issuance costs paid to the lender and reflects debt issuance costs paid to other third parties as other assets. Amortization of debt issuance costs are included as a component of interest expense.

Investment Income and Interest Expense

Investment income consists of interest and dividend income earned on our cash, cash equivalents and short-term investments, along with realized gains (losses) on the sale of investments. Interest expense consists primarily of interest costs and amortization of debt issuance costs related to our debt obligations.

RESULTS OF OPERATIONS

Comparison of the Years Ended December 31, 2015 and 2014

Net Loss

Net loss for the year ended December 31, 2015 was $118.2 million, or ($2.02) per common share—basic and diluted, compared with a net loss of $79.2 million, or ($1.84) per common share—basic and diluted, for the year ended December 31, 2014. The $39.0 million increase in our net loss for the year ended December 31, 2015 as compared to the same period in 2014 was primarily due to:

- Increased research and development expenses of $18.0 million primarily resulting from an increase in clinical trial expenses related to the ARIKAYCE phase 3 CONVERT study and expenses related to research activities for INS1009, and an increase in manufacturing expenses due to production related to our clinical and research programs; and

- Increased general and administrative expenses of $12.1 million resulting from an increase in compensation expenses, including an increase in noncash stock-based compensation related to the vesting of certain performance-based stock options, an increase in pre-commercial expenses in Europe and fees and expenses related to the build-out of our European operations and global tax infrastructure.

In addition, there was an $8.4 million decrease in the benefit from income taxes resulting from the sale of a portion of our New Jersey State net operating losses (NOLs) under the State of New Jersey's Technology Business Tax Certificate Transfer Program for cash of $2.0 million and $10.4 million in 2015 and 2014, respectively, net of commissions. The $10.4 million benefit in 2014 represents two years of sales of NOLs, one in January 2014 and one in December 2014. As of December 31, 2015, we have reached the lifetime maximum allowable amount of NJ NOL sales.

Research and Development Expenses

Research and development expenses for the years ended December 31, 2015 and 2014 were comprised of the following:

	Years Ended December 31,		Increase (decrease)	
	2015	2014	$	%
External Expenses				
Clinical development & research	$ 25,274	$ 12,327	$ 12,947	105.0%
Manufacturing	21,279	16,320	4,959	30.4%
Regulatory and quality assurance	3,051	4,888	(1,837)	(37.6)%
Subtotal—external expenses	$ 49,604	$ 33,535	$ 16,069	47.9%
Internal Expenses				
Compensation and related expenses	$ 18,666	$ 17,543	$ 1,123	6.4%
Other internal operating expenses	6,007	5,214	793	15.2%
Subtotal—internal expenses	$ 24,673	$ 22,757	$ 1,916	8.4%
Total	$ 74,277	$ 56,292	$ 17,985	31.9%

Research and development expenses increased to $74.3 million during the year ended December 31, 2015 from $56.3 million in the same period in 2014. The $18.0 million increase was primarily due to a $13.0 million increase in external clinical development and research expenses related to the ARIKAYCE phase 3 CONVERT study and expenses related to research activities for INS1009. In addition, manufacturing expenses increased $5.0 million primarily due to an increase in production related to our clinical and research programs. We expect research and development expenses to increase in 2016 as compared to 2015 due primarily to the clinical trial activity related to the ARIKAYCE phase 3 CONVERT study.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2015 and 2014 were comprised of the following:

	Year Ended December 31,		Increase (decrease)	
	2015	2014	$	%
General & administrative	$ 30,614	$ 23,032	$ 7,582	32.9%
Pre-commercial expenses	12,602	8,041	4,561	56.7%
Total general & administrative expenses	$ 43,216	$ 31,073	$ 12,143	39.1%

General and administrative expenses increased to $43.2 million during the year ended December 31, 2015 from $31.1 million in the same period in 2014. The $12.1 million increase was primarily due to higher compensation related expenses due to an increase in headcount, an increase in pre-commercial expenses in Europe, a $1.5 million increase in noncash stock-based compensation expense related to certain performance based stock options as the recognition criteria was met upon the MAA for ARIKAYCE being accepted for filing by the EMA in February 2015, and fees and expenses related to the build-out of our European operations and global tax infrastructure. We expect general and administrative expenses to increase in 2016 as compared to 2015 due, in part, to an increase in expenditures related to pre-commercial activities in certain European markets.

Interest Expense

Interest expense was $2.9 million during the year ended December 31, 2015 as compared to $2.4 million in the same period in 2014. The $0.5 million increase in interest expense in 2015 relates to an increase in our borrowings from Hercules. In December 2014, we entered into a third amendment to the Loan and Security Agreement with Hercules which increased our borrowings by an additional $5.0 million to an aggregate total of $25.0 million.

Benefit from Income Taxes

The benefit for income taxes was $2.0 million and $10.4 million for the years ended December 31, 2015 and 2014, respectively. The benefit for income taxes recorded for the year ended December 31, 2014 primarily reflects the reversal of a valuation allowance previously recorded against our New Jersey State net operating losses (NOLs) that resulted from the sale of a portion of our New Jersey State NOLs under the State of New Jersey's Technology Business Tax Certificate Transfer Program (the "Program") for cash of $10.4 million, net of commissions. The Program allows qualified technology and biotechnology businesses in New Jersey to sell unused amounts of NOLs and defined research and development tax credits for cash. The reason for the decrease in tax benefit in 2015 was due to timing, as we recognized the full tax benefits of the 2014 sales of NOLs in calendar year 2014, while the 2013 sales of NOLs were recognized in the first quarter of 2014. In addition in 2015, we reached the lifetime maximum cap of NOLs that can be sold to the State of New Jersey. Therefore we will no longer receive cash proceeds from this program in the future.

Comparison of the Years Ended December 31, 2014 and 2013

Net Loss

Net loss for the year ended December 31, 2014 was $79.2 million, or ($1.84) per common share—basic and diluted, compared with a net loss of $56.1 million, or ($1.60) per common share—basic and diluted for the year ended December 31, 2013. The $23.1 million increase in our net loss in the year ended December 31, 2014 as compared to 2013 was primarily due to $11.5 million in Other revenue received in 2013 related to a one-time payment for the sale of the Company's right to receive future royalties under its license agreement with Premacure (now Shire plc). An increase in 2014 expenses also contributed to the increase in net loss for the period and included a:

- $12.0 million increase in our research and development expenses that primarily resulted from an increase in manufacturing expenses as a result of the build-out of a production area at Therapure's facility, the completion of certain process improvement projects at our third party manufacturing partner and the manufacture of ARIKAYCE for clinical supply. In addition, there was an increase in internal expenses, specifically compensation and personnel related expenses, including non-cash stock compensation expense. These increases were offset, in part, by a decrease in external clinical expenses which was primarily related to the fact that our phase 3 pivotal study in CF patients was completed in 2013; and
- $8.9 million increase in our general and administrative expenses that resulted from an increase in pre-commercial expenses and an increase in certain administrative expenses including an increase in headcount and related compensation expenses and an increase in expenses related to our new headquarters and laboratory facilities in Bridgewater, New Jersey.

Partially offsetting these expenses was a $9.2 million increase in the benefit from income taxes resulting from the sale of a portion of our New Jersey State NOLs under the State of New Jersey's Technology Business Tax Certificate Transfer Program for cash of $10.4 million and $1.2 million in 2014 and 2013, respectively, net of commissions. The $10.4 million benefit from income taxes represents two years of sales of NOLs, one in January 2014 and one in December 2014.

Other Revenue

Other revenue in 2013 solely consisted of a one-time $11.5 million payment we received from Premacure (now Shire plc) in exchange for the Company's right to receive future royalties under its license agreement with Premacure (see Note 10 to the consolidated financial statements on Form 10-K for the year ended December 31, 2014 for additional information regarding our agreement with Premacure). We recorded this as Other revenue in 2013, since all revenue recognition criteria were met and we had no continuing performance obligations related to the payment received.

Research and Development Expenses

Research and development expenses for the year ended December 31, 2014 and 2013 comprised the following:

	Years Ended December 31,		Increase (Decrease)	
	2014	2013	$	%
External Expenses				
Clinical development & research	$ 12,327	$ 19,728	$ (7,401)	-37.5%
Manufacturing	16,320	7,906	8,414	106.4%
Regulatory and quality assurance	4,888	2,010	2,878	143.2%
Subtotal—external expenses	$ 33,535	$ 29,644	$ 3,891	13.1%
Internal Expenses				
Compensation and related expenses	$ 17,543	$ 10,327	$ 7,216	69.9%
Other internal operating expenses	5,214	4,308	906	21.0%
Subtotal—internal expenses	$ 22,757	$ 14,635	$ 8,122	55.5%
Total	$ 56,292	$ 44,279	$ 12,013	27.1%

Research and development expenses increased to $56.3 million during the year ended December 31, 2014 from $44.3 million in the same period in 2013. The $12.0 million increase was primarily due to an $8.4 million increase in manufacturing expenses as a result of the build-out of a production area at Therapure's facility, the completion of certain process improvement projects at our third party manufacturing partner, and the manufacture of ARIKAYCE for clinical supply. In addition, there was an $8.1 million increase in internal expenses, specifically a $7.2 million increase in compensation and related expenses, which included an increase of $2.2 million in stock compensation expenses and additional expenses related to the transition and consulting agreement with our former chief medical officer. These increases were offset, in part, by a decrease of $7.4 million in external clinical expenses which was primarily related to the fact that our phase 3 pivotal study in CF patients was completed in 2013.

General and Administrative Expenses

General and administrative expenses for the years ended December 31, 2014 and 2013 comprised the following:

	December 31,		Increase (Decrease)	
	2014	2013	$	%
General & administrative	$ 23,032	$ 18,627	$ 4,405	23.6%
Pre-commercial expenses	8,041	3,609	4,432	122.8%
Total general & administrative expenses	$ 31,073	$ 22,236	$ 8,837	39.7%

General and administrative expenses increased to $31.1 million during the year ended December 31, 2014 from $22.2 million in the same period in 2013. The $8.9 million increase was primarily due to a $4.5 million increase in pre-commercial expenses and an increase in certain administrative expenses including a $1.8 million increase in headcount and related compensation expense and a $1.5 million increase in expenses related to our new headquarters and laboratory facilities in Bridgewater, New Jersey.

Investment Income and Interest Expense

Investment income was $0.1 million and $0.2 million during the years ended December 31, 2014 and 2013, respectively. Interest expense was $2.4 million during the years ended December 31, 2014 and 2013 and represents interest expense under our Loan Agreement.

Benefit from Income Taxes

The benefit for income taxes was $10.4 million and $1.2 million for the years ended December 31, 2014 and 2013, respectively. The benefit for income taxes recorded for the years ended December 31, 2014 and 2013 solely reflect the reversal of a valuation allowance previously recorded against our New Jersey State NOLs that resulted from the sale of a portion of our New Jersey State NOLs under the State of New Jersey's Technology Business Tax Certificate Transfer Program (the "Program") for cash of $10.4 million and $1.2 million, respectively and net of commissions. The Program allows qualified technology and biotechnology businesses in New Jersey to sell unused amounts of NOLs and defined research and development tax credits for cash. The $10.4 million benefit from income taxes represents two years of sales of NOLs, one in January 2014 and one in December 2014.

LIQUIDITY AND CAPITAL RESOURCES

Overview

There is considerable time and cost associated with developing a potential drug or pharmaceutical product to the point of regulatory approval and commercialization. Historically, we have funded our operations through public and private placements of equity securities, through debt financing, from the proceeds from the sale of our follow-on biologics platform to Merck in 2009 and from revenues related to sales of product and our IPLEX expanded access program, which was discontinued in 2011. We expect to continue to incur losses because we plan to fund research and development activities and commercial launch activities, and we do not expect material revenues for at least the next two years.

We believe we currently have sufficient funds to meet our financial needs for at least the next twelve months. We may opportunistically raise additional capital and may do so through equity or debt financing(s), strategic transactions or otherwise. Such additional funding will be necessary to continue to develop our potential product candidates, to pursue the license or purchase of other technologies, to commercialize our product candidates or to purchase other products. We cannot assure you that adequate capital will be available on favorable terms, or at all, when needed. If we are unable to obtain sufficient additional funds when required, we may be forced to delay, restrict or eliminate all or a portion of our research or development programs, dispose of assets or technology or cease operations. During the remainder of 2016, we plan to continue to fund further clinical development of ARIKAYCE and INS1009, support efforts to obtain regulatory approvals and prepare for commercialization in certain European countries. Our cash requirements in 2016 will be impacted by a number of factors,

the most significant of which, being the enrollment rates and other expenses related to the CONVERT study.

On April 6, 2015, we completed an underwritten public offering of 11.5 million shares of our common stock, which included the underwriter's exercise in full of its over-allotment option of 1.5 million shares, at a price to the public of $20.65 per share. Our net proceeds from the sale of the shares, after deducting the underwriter's discount and offering expenses of $14.5 million, were $222.9 million.

Cash Flows

As of December 31, 2015, we had total cash and cash equivalents of $282.9 million, as compared with $159.2 million as of December 31, 2014. The $123.7 million increase was due primarily to net proceeds received from the issuance of 11.5 million shares of our common stock in April 2015 offset by the use of cash in operating activities. Our working capital was $265.9 million as of December 31, 2015.

Net cash used in operating activities was $100.7 million and $64.4 million for the years ended December 31, 2015 and 2014, respectively. The net cash used in operating activities during 2015 and 2014 was primarily for the clinical, regulatory and pre-commercial activities related to ARIKAYCE.

Net cash used in investing activities was $3.5 million and $5.3 million for the years ended December 31, 2015 and 2014, respectively. The net cash used in investing activities during 2015 was primarily related to payments for the build out of our headquarters and lab facility in Bridgewater, New Jersey, as well as investments in an enterprise resource planning software system.

Net cash provided by financing activities was $227.8 million and $115.1 million for the years ended December 31, 2015 and 2014, respectively. Net cash provided by financing activities in 2015 included net proceeds of $222.9 million received from the issuance of 11.5 million common shares in April 2015 and proceeds of $5.1 million received from stock option exercises. Net cash provided by financing activities in 2014 included $109.0 million from the issuance of common stock.

Contractual Obligations

On June 29, 2012, we and our domestic subsidiaries, as co-borrowers, entered into a Loan and Security Agreement with Hercules that allowed us to borrow up to $20.0 million ("Loan Agreement") at an interest rate of 9.25%. On December 15, 2014, we entered into a third amendment (the "Third Amendment") to the Loan Agreement with Hercules. In connection with the Third Amendment, we paid a commitment fee of $25,000, and at the closing, paid a facility fee of $125,000. Under the Third Amendment, the amount of borrowings was increased by an additional $5.0 million to an aggregate total of $25.0 million and the interest-only period was extended through December 31, 2015. In December 2015, we entered into a fifth amendment to the Loan Agreement to exercise an option to extend the maturity date of the loan to January 1, 2018 with a payment to Hercules of $250,000. The amendment extends the interest-only period, with principal repayments beginning in October 2016.

We have an operating lease for office and laboratory space located in Bridgewater, NJ, our corporate headquarters, for which the initial lease term expires in November 2019. Future minimum rental payments under this lease total approximately $3.8 million. We hold a lease that expires in October 2016 for office space in Richmond, VA, the site of our former corporate headquarters. Future minimum rental payments under this lease total approximately $0.4 million. During 2011, we recorded a net present value charge of $1.2 million in general and administrative expenses associated with

vacating the Richmond facility. In November 2014, we entered into an agreement to sublet this space for the remainder of the lease term. We expect to collect proceeds from the sublease in the amount of $0.2 million over the remaining term of the lease.

In September 2015, we entered into a Commercial Fill/Finish Services Agreement (the "Fill/Finish Agreement") with Ajinomoto Althea, Inc., a Delaware corporation ("Althea"), for Althea to produce, on a non-exclusive basis, ARIKAYCE in finished dosage form. Under the Fill/Finish Agreement, we are obligated to pay a minimum of $2.7 million for the batches of ARIKAYCE produced each calendar year during the term of the Fill/Finish Agreement. The Fill/Finish Agreement is effective as of January 1, 2015, has an initial term that ends on December 31, 2017 and may be extended for additional two year periods upon mutual written agreement of the Company and Althea at least one year prior to the expiration of its then-current term.

As of December 31, 2015, future payments under our long-term debt agreements, capital leases, minimum future payments under non-cancellable operating leases (net of sublease) and minimum future payment obligations are as follows:

	As of December 31, 2015 Payments Due By Period				
	Total	Less than 1 year	1 - 3 Years	4 - 5 Years	After 5 Years
			(In thousands)		
Debt obligations					
Debt maturities	$ 25,000	$ 2,873	$ 22,127	$ -	$ -
Contractual interest	4,358	2,719	1,639	-	-
Operating leases	4,256	1,271	2,021	964	-
Purchase obligations	5,400	2,700	2,700	-	-
Total contractual obligations	$ 39,014	$ 9,563	$ 28,487	$ 964	$ -

This table does not include: (a) any milestone payments which may become payable to third parties under our license and collaboration agreements as the timing and likelihood of such payments are not known; (b) any royalty payments to third parties as the amounts of such payments, timing and/or the likelihood of such payments are not known; (c) contracts that are entered into in the ordinary course of business which are not material in the aggregate in any period presented above; or (d) any payments related to the agreements mentioned below.

We currently have a licensing agreement with PARI for the use of the optimized eFlow Nebulizer System for delivery of ARIKAYCE in treating patients with NTM infections, CF and bronchiectasis. We have rights to several US and foreign issued patents, and patent applications involving improvements to the optimized eFlow Nebulizer System. Under the licensing agreement, PARI is entitled to receive payments either in cash, qualified stock or a combination of both, at PARI's discretion, based on achievement of certain milestone events including phase 3 trial initiation (which occurred in 2012), first acceptance of MAA submission (or equivalent) in the US of ARIKAYCE and the device, first receipt of marketing approval in the US for ARIKAYCE and the device, and first receipt of marketing approval in a major EU country for ARIKAYCE and the device. In addition, PARI is entitled to receive royalty payments in the mid-single digits on commercial net sales of ARIKAYCE pursuant to the licensing agreement, subject to certain specified annual minimum royalties. In July 2014, we entered into a Commercialization Agreement (the "PARI Agreement") with PARI for the manufacture and supply of eFlow nebulizer systems and related accessories (the "Device") as optimized for use with our proprietary liposomal amikacin for inhalation. The PARI Agreement has an initial term of fifteen years from the first commercial sale of ARIKAYCE pursuant to the licensing

agreement (the "Initial Term"). The term of the PARI Agreement may be extended by us for an additional five years by providing written notice to PARI at least one year prior to the expiration of the Initial Term.

In 2004 and 2009, we entered into research funding agreements with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) whereby we received $1.7 million and $2.2 million for each respective agreement in research funding for the development of ARIKAYCE. If ARIKAYCE becomes an approved product for CF patients in the US, we will owe a payment to CFFT of up to $13.4 million that is payable over a three-year period after approval as a commercialized drug in the US. Furthermore, if certain global sales milestones are met within 5 years of the drug commercialization, we would owe an additional $3.9 million in additional payments. Since there is significant development risk associated with ARIKAYCE, we have not accrued these obligations.

In February 2014, we entered into a contract manufacturing agreement with Therapure for the manufacture of ARIKAYCE at the larger scales necessary to support commercialization. Pursuant to the agreement, we collaborated with Therapure to construct a production area for the manufacture of ARIKAYCE in Therapure's existing manufacturing facility in Mississauga, Ontario, Canada. We paid Therapure approximately $12 million for the build out of the construction area and related manufacturing costs. Therapure will manufacture ARIKAYCE for us on a non-exclusive basis. The agreement has an initial term of five years from the first date on which Therapure delivers ARIKAYCE to us after we obtain permits related to the manufacture of ARIKAYCE. Under the agreement, we are obligated to pay certain minimum amounts for the batches of ARIKAYCE produced each calendar year.

In December 2014, we entered into Work Order 1 (the "Work Order"), pursuant to a Master Agreement for Services with SynteractHCR, Inc. ("Synteract") dated as of August 27, 2014, as amended on December 23, 2014, pursuant to which we retained Synteract to perform implementation and management services in connection with certain clinical trials pursuant to a specific protocol of pharmaceutical products under development by us or under our control. Synteract is providing comprehensive services for protocol INS-212, a randomized, open-label, multicenter study of liposomal amikacin for inhalation in adult patients with NTM lung infections caused by MAC complex that are refractory to treatment. Prior to the execution of the Work Order, Synteract was providing such services pursuant to a Letter of Intent, dated August 25, 2014. We anticipate that aggregate costs relating to all work orders for the 212 study will be approximately $40 million over the period of the study. In April 2015, we entered into a work order with Synteract to perform implementation and management services for protocol INS-312, a study in which all non-converters from the INS-212 study will be eligible to enter a separate open-label study. We anticipate that aggregate costs relating to all work orders for the 312 study will be approximately $20 million over the period of the study.

Future Funding Requirements

We will need to raise additional capital to fund our operations, to develop and commercialize ARIKAYCE, to develop INS1009, and to develop, acquire, in-license or co-promote other products that address orphan or rare diseases. Our future capital requirements may be substantial and will depend on many factors, including:

- the timing and cost of our anticipated clinical trials of ARIKAYCE for the treatment of patients with NTM lung infections;

- the decisions of the FDA and EMA with respect to our applications for marketing approval of ARIKAYCE in the US and Europe; the costs of activities related to the regulatory approval process; and the timing of approvals, if received;
- the cost of putting in place the sales and marketing capabilities necessary to be prepared for a potential commercial launch of ARIKAYCE, if approved;
- the cost of filing, prosecuting and enforcing patent claims;
- the costs of our manufacturing-related activities;
- the costs associated with commercializing ARIKAYCE if we receive marketing approval; and
- subject to receipt of marketing approval, the levels, timing and collection of revenue received from sales of approved products, if any, in the future.

In April 2015, we generated net proceeds of $222.9 million from the issuance of 11.5 million shares of common stock. We believe we currently have sufficient funds to meet our financial needs for the next twelve months. However, our business strategy may require us to, or we may otherwise determine to, raise additional capital at any time through equity or debt financing(s), strategic transactions or otherwise. Such additional funding may be necessary to continue to develop our potential product candidates, to pursue the license or purchase of complementary technologies, to commercialize our product candidates or to purchase other products. If we are unable to obtain additional financing, we may be required to reduce the scope of our planned product development and commercialization or our plans to establish a sales and marketing force, any of which could harm our business, financial condition and results of operations. The source, timing and availability of any future financing will depend principally upon equity and debt market conditions, interest rates and, more specifically, our continued progress in our regulatory, development and commercial activities. We cannot assure you that such capital funding will be available on favorable terms or at all. If we are unable to obtain sufficient additional funds when required, we may be forced to delay, restrict or eliminate all or a portion of our research or development programs, dispose of assets or technology or cease operations.

To date, we have not generated any meaningful revenue from ARIKAYCE. We do not know when or if we will generate any revenue. We do not expect to generate significant revenue unless or until we obtain marketing approval of, and commercialize, ARIKAYCE.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements, other than operating leases, that have or are reasonably likely to have a current or future material effect on our financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources. We do not have any interest in special purpose entities, structured finance entities or other variable interest entities.

CRITICAL ACCOUNTING POLICIES

Preparation of financial statements in accordance with generally accepted accounting principles in the US requires us to make estimates and assumptions affecting the reported amounts of assets, liabilities, revenues and expenses and the disclosures of contingent assets and liabilities. We use our historical experience and other relevant factors when developing our estimates and assumptions. We continually evaluate these estimates and assumptions. The amounts of assets and liabilities reported in our consolidated balance sheets and the amounts of revenue reported in our consolidated statements of comprehensive loss are effected by estimates and assumptions, which are used for, but not limited to, the accounting for research and development, revenue recognition, stock-based compensation, identifiable intangible assets and goodwill, and accrued expenses. The accounting policies discussed below are considered critical to an understanding of our consolidated financial statements because their

application places the most significant demands on our judgment. Actual results could differ from our estimates. For additional accounting policies, see Note 2 to our Consolidated Financial Statements—"Summary of Significant Accounting Policies."

Research and Development

Research and development expenses consist primarily of salaries, benefits and other related costs, including stock-based compensation, for personnel serving our research and development functions, and other internal operating expenses, the cost of manufacturing our drug candidate for clinical study, the cost of conducting clinical studies, and the cost of conducting preclinical and research activities. Our expenses related to manufacturing our drug candidate for clinical study are primarily related to activities at contract manufacturing organizations that manufacture ARIKAYCE and INS1009 for our use. Our expenses related to clinical trials are primarily related to activities at contract research organizations that conduct and manage clinical trials on our behalf. These contracts set forth the scope of work to be completed at a fixed fee or amount per patient enrolled. Payments under these contracts depend on performance criteria such as the successful enrollment of patients or the completion of clinical trial milestones as well as time-based fees. Expenses are accrued based on contracted amounts applied to the level of patient enrollment and to activity according to the clinical trial protocol.

Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are then recognized as an expense as the related goods are delivered or the services are performed, or when the goods or services are no longer expected to be provided.

Revenue Recognition

In the periods when we record revenue, we recognize revenues when all of the following four criteria are present: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectability is reasonably assured. We did not record any material revenue for the years ended December 31, 2015 and 2014.

Where we have continuing performance obligations under the terms of a collaborative arrangement, non-refundable upfront license payments received upon contract signing are recorded as deferred revenue and recognized as revenue as the related activities are performed. The period over which these activities are to be performed is based upon management's estimate of the development period. Changes in management's estimate could change the period over which revenue is recognized. Research and/or development payments are recognized as revenues as the related research and/or development activities are performed and when we have no continuing performance obligations related to the research and development payment received.

Where we have no continuing involvement under a collaborative arrangement, we record nonrefundable license fee revenues when we have the contractual right to receive the payment, in accordance with the terms of the collaboration agreement, and record milestones upon appropriate notification to us of achievement of the milestones by the collaborative partner.

We recognize revenue from milestone payments when earned, provided that (i) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement and (ii) we do not have ongoing performance obligations related to the achievement of the milestone earned. Milestone payments are considered substantive if all of the following conditions are met: the milestone payment (a) is commensurate with either the vendor's performance to achieve the milestone or the enhancement of the value of the delivered item or items as a result of a specific outcome

resulting from the vendor's performance to achieve the milestone, (b) relates solely to past performance, and (c) is reasonable relative to all of the deliverables and payment terms (including other potential milestone consideration) within the arrangement. Any amounts received under the agreement in advance of performance, if deemed substantive, are recorded as deferred revenue and recognized as revenue as we complete our performance obligations.

With regard to recognizing revenue for multiple deliverable revenue arrangements, each deliverable within a multiple-deliverable revenue arrangement is accounted for as a separate unit of accounting if both of the following criteria are met: (1) the delivered item or items have value to the customer on a standalone basis and (2) for an arrangement that includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in our control.

In addition, multiple deliverable revenue arrangement consideration is allocated at the inception of an arrangement to all deliverables using the relative selling price method. We also apply a selling price hierarchy for determining the selling price of a deliverable, which includes (1) vendor- specific objective evidence, if available, (2) third-party evidence, if vendor-specific objective evidence is not available, and (3) estimated selling price if neither vendor-specific nor third-party evidence is available.

Deferred revenue associated with a non-refundable payment received under a collaborative agreement that is terminated prior to its completion results in an immediate recognition of the deferred revenue.

Stock-Based Compensation

We recognize stock-based compensation expense for awards of equity instruments to employees and directors based on the grant-date fair value of those awards. The grant-date fair value of the award is recognized as compensation expense ratably over the requisite service period, which generally equals the vesting period of the award, and if applicable, is adjusted for expected forfeitures. We also grant performance-based stock options to employees. The grant-date fair value of the performance-based stock options is recognized as compensation expense over the implicit service period using the accelerated attribution method once it is probable that the performance condition will be achieved. Stock-based compensation expense is included in both research and development expenses and general and administrative expenses in the Consolidated Statements of Comprehensive Loss. For awards that were deemed to be granted outside of the Company's 2000 Stock Incentive Plan, we used liability accounting. These awards were classified as a liability and were remeasured at fair value at the end of each reporting period. Changes in fair value are included in compensation expense in the Consolidated Statements of Comprehensive Loss (see additional disclosures related to awards granted outside of the 2000 Stock Incentive Plan in Footnote 8 "Stock-Based Compensation" of our consolidated financial statements located in Part IV, Item 15 of this Annual Report on Form 10-K).

The following table summarizes the assumptions used in determining the fair value of stock options granted during the years ended December 31, 2015, 2014 and 2013:

	2015	2014	2013
Volatility	78% - 82%	83% - 86%	86% - 96%
Risk-free interest rate	1.31% - 1.75%	1.46% - 1.83%	0.65% - 1.65%
Dividend yield	0.0%	0.0%	0.0%
Expected option term (in years)	6.25	6.25	6.25

For the years ended December 31, 2015, 2014 and 2013, the volatility factor was based on our historical volatility since the closing of our merger with Transave, Inc. on December 1, 2010. The expected life was determined using the simplified method as described in ASC Topic 718, "Accounting for Stock Compensation", which is the midpoint between the vesting date and the end of the contractual term. The risk-free interest rate is based on the US Treasury yield in effect at the date of grant. Forfeitures are based on actual percentage of option forfeitures since the closing of the merger on December 1, 2010 and are the basis for future forfeiture expectations.

Identifiable Intangible Assets

Identifiable intangible assets are measured at their respective fair values and are not amortized until commercialization. Once commercialization occurs, these intangible assets will be amortized over their estimated useful lives. The fair values assigned to our intangible assets are based on reasonable estimates and assumptions given available facts and circumstances. Unanticipated events or circumstances may occur that may require us to review the assets for impairment. Events or circumstances that may require an impairment assessment include negative clinical trial results, the non-approval of a new drug application by a regulatory agency, material delays in our development program or a sustained decline in market capitalization.

Indefinite-lived intangible assets are not subject to periodic amortization. Rather, indefinite-lived intangibles are reviewed for impairment by applying a fair value based test on an annual basis or more frequently if events or circumstances indicate impairment may have occurred. Events or circumstances that may require an interim impairment assessment are consistent with those described above. We perform our annual impairment test as of October 1 of each year.

We use the income approach to derive the fair value of in-process research and development assets. This approach calculates fair value by estimating future cash flows attributable to the assets and then discounting these cash flows to a present value using a risk-adjusted discount rate. A market based valuation approach was not considered given a lack of revenues and profits by us. This approach requires significant management judgment with respect to unobservable inputs such as future volume, revenue and expense growth rates, changes in working capital use, appropriate discount rates and other assumptions and estimates. The estimates and assumptions used are consistent with our business plans.

Accrued Expenses

We are required to estimate accrued expenses as part of our process of preparing financial statements. This process involves estimating the level of service performed on our behalf and the associated cost incurred in instances where we have not been invoiced or otherwise notified of actual costs. Examples of areas in which subjective judgments may be required include costs associated with services provided by contract organizations for preclinical development, clinical trials and manufacturing of clinical materials. We accrue for expenses associated with these external services by determining the total cost of a given study based on the terms of the related contract. We accrue for costs incurred as the services are being provided by monitoring the status of the trials and the invoices received from our external service providers. In the case of clinical trials, the estimated cost normally relates to the projected costs of having subjects enrolled in our trials, which we recognize over the estimated term of the trial according to the number of subjects enrolled in the trial on an ongoing basis, beginning with subject enrollment. As actual costs become known to us, we adjust our accruals. To date, the number of clinical trials and related research service agreements has been relatively limited and our estimates have not differed significantly from the actual costs incurred.

New Accounting Pronouncements

In April 2015, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2015-03, Simplifying the Presentation of Debt Issuance Costs. The new standard requires that debt issuance costs be presented in the balance sheet as a direct reduction from the carrying value of the associated debt liability, consistent with the presentation of a debt discount. The standard is effective for public entities for annual and interim periods beginning after December 15, 2015. Early adoption is permitted for financial statements that have not been previously issued. The new guidance will be applied on a retrospective basis. We have determined the impact of this standard will be not be material on our consolidated results of operations and financial position.

In November 2015, the FASB issued ASU 2015-17, Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes, which updated and simplified the presentation of deferred income taxes. Current generally accepted accounting principles require an entity to separate deferred income tax liabilities and assets into current and noncurrent amounts in a classified statement of financial position. To simplify the presentation of deferred income taxes, the amendments in this update require that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position. The current requirement that deferred tax assets and liabilities of a tax-paying component of an entity be offset and presented as a single amount is not affected by the amendments in this update. The amendments in this update are effective for financial statements issued for annual periods beginning after December 15, 2016 and interim periods within those annual periods. Earlier application is permitted as of the beginning of an interim or annual reporting period. We have early adopted the update effective with its annual reporting period ended December 31, 2015. The adoption of this update did not have a significant impact on our consolidated financial statements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As of December 31, 2015, our cash and cash equivalents were in cash accounts or were invested in money funds. Such accounts or investments are not insured by the federal government.

As of December 31, 2015, we had $25.0 million of fixed rate borrowings bearing interest at 9.25% outstanding under a Loan and Security Agreement we entered into in June 2012 and amended most recently in December 2015. If a 10% change in interest rates was to have occurred on December 31, 2015, this change would not have had a material effect on the fair value of our debt as of that date, nor would it have had a material effect on our future earnings or cash flows.

The majority of our business is conducted in US dollars. However, we do conduct certain transactions in other currencies, including Euros, British Pounds and Japanese Yen. Fluctuations in foreign currency exchange rates do not materially affect our results of operations. During 2015, 2014 and 2013, our results of operations were not materially affected by fluctuations in foreign currency exchange rates.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by Item 8 is included in our Financial Statements and Supplementary Data listed in Item 15 of Part IV of this Annual Report on Form 10-K.

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

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2015. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d- 15(e) under the Exchange Act, means controls and other procedures that are designed to provide reasonable assurance that information required to be disclosed by us in the periodic reports that we file or submit with the SEC is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and to ensure that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. Based on that evaluation, as of December 31, 2015, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures are effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended, as a process designed by, or under the supervision of, our principal executive and principal financial and accounting officers and effected by our board of directors and management 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 the transactions and dispositions of our assets;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with US generally accepted accounting principles, and that receipts and expenditures of our company are being made only in accordance with authorizations of our management and board of 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 the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risks that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2015, based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control—Integrated Framework (2013 framework). A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of a company's annual or interim financial statements will not be prevented or detected on a timely basis. Based on management's assessment, management concluded that the Company's internal control over financial reporting was effective as of December 31, 2015.

Ernst & Young LLP, our independent registered public accounting firm, issued an attestation report on our internal control over financial reporting. The report of Ernst & Young LLP is contained in Item 15 of Part IV of this Annual Report on Form 10-K.

ITEM 9B. OTHER INFORMATION

None

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Pursuant to General Instruction G(3) of Form 10-K, the information required by Item 10 of Form 10-K is hereby incorporated by reference from the discussion responsive thereto under the captions "Election of Directors," "Corporate Governance" and "Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive proxy statement for our 2016 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report.

ITEM 11. EXECUTIVE COMPENSATION

Pursuant to General Instruction G(3) of Form 10-K, the information required by Item 11 of Form 10-K is hereby incorporated by reference from the discussion responsive thereto under the captions "Compensation Discussion and Analysis," "Compensation Committee Report," "Compensation Committee Interlocks and Insider Participation" and "Directors Compensation" in our definitive proxy statement for our 2016 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report.

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

Pursuant to General Instruction G(3) of Form 10-K, the information required by Item 12 of Form 10-K is hereby incorporated by reference from the discussion responsive thereto under the captions "Compensation Discussion and Analysis," "Security Ownership of Certain Beneficial Owners" and "Security Ownership of Directors and Management" in our definitive proxy statement for our 2016 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS AND DIRECTOR INDEPENDENCE

Pursuant to General Instruction G(3) of Form 10-K, the information required by Item 13 of Form 10-K is hereby incorporated by reference from the discussion responsive thereto under the captions "Election of Directors" and "Certain Relationships and Related Transactions" in our definitive proxy statement for our 2016 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Pursuant to General Instruction G(3) of Form 10-K, the information required by Item 14 of Form 10-K is hereby incorporated by reference from the discussion responsive thereto under the caption "Corporate Governance" and "Ratification of Independent Public Accountants" in our definitive proxy statement for our 2016 annual meeting of shareholders to be filed with the SEC no later than 120 days after the close of the fiscal year covered by this Annual Report.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) Documents filed as part of this report.

1. FINANCIAL STATEMENTS . The following consolidated financial statements of the Company are set forth herein, beginning on page 93:

(i) Reports of Independent Registered Public Accounting Firm

(ii) Consolidated Balance Sheets as of December 31, 2015 and 2014

(iii) Consolidated Statements of Comprehensive Loss for the Years Ended December 31, 2015, 2014 and 2013

(iv) Consolidated Statements of Stockholders' Equity for the Years Ended December 31, 2015, 2014 and 2013

(v) Consolidated Statements of Cash Flows for the Years Ended December 31, 2015, 2014 and 2013

(vi) Notes to Consolidated Financial Statements

2. FINANCIAL STATEMENT SCHEDULES.

None required.

3. EXHIBITS.

The exhibits that are required to be filed or incorporated by reference herein are listed in the Exhibit Index.

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 on February 25, 2016.

INSMED INCORPORATED
a Virginia corporation
(Registrant)

By: /s/ WILLIAM H. LEWIS

William H. Lewis
President and Chief Executive Officer (Principal Executive Officer) and Director

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 indicated on February 25, 2016.

Signature	Title
/s/ WILLIAM H. LEWIS William H. Lewis	President and Chief Executive Officer (Principal Executive Officer) and Director
/s/ ANDREW T. DRECHSLER Andrew T. Drechsler	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)
/s/ DONALD HAYDEN, JR. Donald Hayden, Jr.	Chairman of the Board of Directors
/s/ ALFRED F. ALTOMARI Alfred F. Altomari	Director
/s/ DAVID R. BRENNAN David R. Brennan	Director
/s/ STEINAR J. ENGELSEN, M.D. Steinar J. Engelsen, M.D.	Director
/s/ DAVID W.J. MCGIRR David W.J. McGirr	Director
/s/ MYRTLE POTTER Myrtle Potter	Director
/s/ MELVIN SHAROKY, M.D. Melvin Sharoky, M.D.	Director

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Insmed Incorporated

We have audited the accompanying consolidated balance sheets of Insmed Incorporated as of December 31, 2015 and 2014, and the related consolidated statements of comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2015. 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as 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 consolidated financial position of Insmed Incorporated at December 31, 2015 and 2014, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Insmed Incorporated's internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 25, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Iselin, New Jersey
February 25, 2016

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of Insmed Incorporated

We have audited Insmed Incorporated's internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control —Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Insmed Incorporated's management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

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

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

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

In our opinion, Insmed Incorporated maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Insmed Incorporated as of December 31, 2015 and 2014, and the related consolidated statements of comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2015 and our report dated February 25, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Iselin, New Jersey
February 25, 2016

INSMED INCORPORATED
Consolidated Balance Sheets
(in thousands, except par value and share data)

	As of December 31,	
	2015	**2014**
Assets		
Current assets:		
Cash and cash equivalents	$ 282,876	$ 159,226
Prepaid expenses and other current assets	5,242	5,488
Total current assets	288,118	164,714
In-process research and development	58,200	58,200
Fixed assets, net	8,092	7,534
Other assets	2,146	416
Total assets	$ 356,556	$ 230,864
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 7,468	$ 9,249
Accrued expenses	10,995	9,638
Other current liabilities	683	743
Current portion of long-term debt	3,113	-
Total current liabilities	22,259	19,630
Long-term liabilities:		
Accrued lease expense, long-term	-	118
Other long-term liabilities	572	23
Debt, long-term	22,027	24,856
Total liabilities	44,858	44,627
Common stock, $0.01 par value; 500,000,000 authorized shares, 61,813,995 and 49,806,131 issued and outstanding shares at December 31, 2015 and December 31, 2014, respectively	618	498
Additional paid-in capital	900,043	656,519
Accumulated deficit	(588,963)	(470,780)
Total shareholders' equity	311,698	186,237
Total liabilities and shareholders' equity	$ 356,556	$ 230,864

See accompanying notes to consolidated financial statements

INSMED INCORPORATED
Consolidated Statements of Comprehensive Loss
(in thousands, except per share data)

	Years ended December 31,		
	2015	**2014**	**2013**
Other revenue	$ -	$ -	$ 11,500
Total revenues	-	-	11,500
Operating expenses:			
Research and development	74,277	56,292	44,279
General and administrative	43,216	31,073	22,236
Total operating expenses	117,493	87,365	66,515
Operating loss	(117,493)	(87,365)	(55,015)
Investment income	261	58	166
Interest expense	(2,889)	(2,415)	(2,412)
Other income/(expense), net	(33)	141	(33)
Loss before income taxes	(120,154)	(89,581)	(57,294)
Benefit from income taxes	(1,971)	(10,422)	(1,221)
Net loss and comprehensive loss	$ (118,183)	$ (79,159)	$ (56,073)
Basic and diluted net loss per share	$ (2.02)	$ (1.84)	$ (1.60)
Weighted average basic and diluted common shares outstanding	58,633	43,095	34,980

See accompanying notes to audited consolidated financial statements

INSMED INCORPORATED
Consolidated Statements of Stockholders' Equity
(in thousands)

	Common Stock		Warrant		Additional Paid-in Capital	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount			
Balance at January 1, 2013	31,488	$ 315	330	$ 790	$ 455,325	$ (335,548)	$ 120,882
Comprehensive loss:							
Net loss						(56,073)	(56,073)
Exercise of stock options	372	4			1,622		1,626
Net proceeds from issuance of common stock	6,900	69			66,948		67,017
Issuance of common stock for vesting of RSUs	154	1			(1)		-
Exercise of warrants	223	2	(330)	(790)	788		-
Reclass of stock compensation expense for liability awards to equity					3,371		3,371
Stock compensation expense					6,501		6,501
Balance at December 31, 2013	39,137	$ 391	-	$ -	$ 534,554	$ (391,621)	$ 143,324
Comprehensive loss:							
Net loss						(79,159)	(79,159)
Exercise of stock options	283	3			1,728		1,731
Net proceeds from issuance of common stock	10,306	103			108,910		109,013
Issuance of common stock for vesting of RSUs	80	1			(1)		-
Stock compensation expense					11,328		11,328
Balance at December 31, 2014	49,806	$ 498	-	$ -	$ 656,519	$ (470,780)	$ 186,237
Comprehensive loss:							
Net loss						(118,183)	(118,183)
Exercise of stock options	481	5			5,107		5,112
Net proceeds from issuance of common stock	11,500	115			222,827		222,942
Issuance of common stock for vesting of RSUs	27						-
Stock compensation expense					15,590		15,590
Balance at December 31, 2015	61,814	$ 618	-	$ -	$ 900,043	$ (588,963)	$ 311,698

See accompanying notes to audited consolidated financial statements

INSMED INCORPORATED
Consolidated Statements of Cash Flows
(in thousands)

	Years ended December 31,		
	2015	**2014**	**2013**
Operating activities			
Net loss	$ (118,183)	$ (79,159)	$ (56,073)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,982	1,073	680
Stock based compensation expense	15,590	11,328	8,668
Loss / (gain) on sale of assets, net	-	9	(2)
Amortization of debt discount and debt issuance costs	458	390	333
Accrual of the end of term charge on the debt	76	110	160
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	(1,484)	(2,972)	(1,832)
Accounts payable	(1,781)	3,312	(1,131)
Accrued expenses and other	2,642	1,493	2,533
Net cash used in operating activities	(100,700)	(64,416)	(46,664)
Investing activities			
Purchase of fixed assets	(3,454)	(5,351)	(826)
Proceeds from sale of asset	-	10	2
Maturity of a certificate of deposit	-	-	2,153
Net cash (used in) / provided by investing activities	(3,454)	(5,341)	1,329
Financing activities			
Payments on capital lease obligations	-	(64)	(96)
Proceeds from issuance of debt	-	5,000	-
Proceeds from issuance of common stock	222,942	109,013	67,017
Proceeds from exercise of stock options	5,112	1,390	1,626
Payment of debt issuance costs	(250)	(250)	(100)
Net cash provided by financing activities	227,804	115,089	68,447
Increase in cash and cash equivalents	123,650	45,332	23,112
Cash and cash equivalents at beginning of period	159,226	113,894	90,782
Cash and cash equivalents at end of period	$ 282,876	$ 159,226	$ 113,894
Supplemental disclosures of cash flow information:			
Cash paid for interest	$ 2,948	$ 1,803	$ 1,809
Cash received for taxes, net	$ 3,008	$ 9,429	$ 1,221
Supplemental disclosures of non-cash investing and financing activities:			
Value of warrant exercised by converting the warrant into shares of common stock ("net issuance method")	$ -	$ -	$ 790

See accompanying notes to audited consolidated financial statements

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Description of Business and Basis of Presentation

Description of Business —Insmed is a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. The Company's lead product candidate is ARIKAYCE, or liposomal amikacin for inhalation (LAI), which is in late-stage development for patients with nontuberculous mycobacteria (NTM) lung disease, a rare and often chronic infection that is capable of causing irreversible lung damage and which can be fatal. The Company's earlier stage pipeline includes INS1009, a nebulized prodrug formulation of treprostinil.

The Company was incorporated in the Commonwealth of Virginia on November 29, 1999 and its principal executive offices are located in Bridgewater, New Jersey. During 2015 the Company formed subsidiaries in a number of countries in Europe in preparation for the commercialization of ARIKAYCE, upon approval in the European Union, and to support its global tax structure. The Company has operations in the United States (US), Ireland, Germany, France, the United Kingdom and the Netherlands.

Basis of Presentation —The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Transave, LLC, Insmed Pharmaceuticals, Inc., Insmed Limited, Celtrix Pharmaceuticals, Inc., Insmed Holdings Limited, Insmed Ireland Limited, Insmed France SAS, Insmed Germany GmbH and Insmed Netherlands B.V. All intercompany transactions and balances have been eliminated in consolidation.

2. Summary of Significant Accounting Policies

Use of Estimates —The preparation of the consolidated financial statements in conformity with accounting principles generally accepted in the United States (GAAP) requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. The Company bases its estimates and judgments on historical experience and on various other assumptions. The amounts of assets and liabilities reported in the Company's balance sheets and the amounts of expenses reported for each period presented are effected by estimates and assumptions, which are used for, but not limited to, the accounting for stock-based compensation, income taxes, loss contingencies, and accounting for research and development costs. Actual results could differ from those estimates.

Investment Income and Interest Expense —Investment income consists of interest and dividend income earned on the Company's cash, cash equivalents and short-term investments, along with realized gains (losses) on the sale of investments. Interest expense consists primarily of interest costs related to the Company's debt.

Cash and Cash Equivalents —The Company considers cash equivalents to be highly liquid investments with maturities of three months or less from the date of purchase.

Fixed Assets, Net —Fixed assets are recorded at cost and are depreciated on a straight-line basis over the estimated useful lives of the assets. Estimated useful lives of three to five years are used for computer equipment. Estimated useful lives of seven years are used for laboratory equipment, office equipment and furniture and fixtures. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the asset. Long-lived assets are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

2. Summary of Significant Accounting Policies (Continued)

recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated future cash flows, then an impairment charge is recognized for the amount by which the carrying value of the asset exceeds the fair value of the asset.

Identifiable Intangible Assets —Identifiable intangible assets are measured at their respective fair values and are not amortized until commercialization. Once commercialization occurs, these intangible assets will be amortized over their estimated useful lives. The fair values assigned to the Company's intangible assets are based on reasonable estimates and assumptions given available facts and circumstances. Unanticipated events or circumstances may occur that may require the Company to review the assets for impairment. Events or circumstances that may require an impairment assessment include negative clinical trial results, the non-approval of a new drug application by a regulatory agency, material delays in the Company's development program or a sustained decline in market capitalization.

Indefinite-lived intangible assets are not subject to periodic amortization. Rather, indefinite-lived intangibles are reviewed for impairment by applying a fair value based test on an annual basis or more frequently if events or circumstances indicate impairment may have occurred. Events or circumstances that may require an interim impairment assessment are consistent with those described above. The Company performs its annual impairment test as of October 1 of each year.

The Company uses the income approach to derive the fair value of in- process research and development assets. This approach calculates fair value by estimating future cash flows attributable to the assets and then discounting these cash flows to a present value using a risk-adjusted discount rate. A market based valuation approach was not considered given a lack of revenues and profits for the Company. This approach requires significant management judgment with respect to unobservable inputs such as future volume, revenue and expense growth rates, changes in working capital use, appropriate discount rates and other assumptions and estimates. The estimates and assumptions used are consistent with the Company's business plans.

Debt Issuance Costs —Debt issuance costs are amortized using the effective interest rate method and amortized to interest expense over the term of the debt. Debt issuance costs paid to the lender are reflected as a discount to the debt, and debt issuance costs paid to other third parties are reflected as other assets in the consolidated balance sheets.

Fair Value Measurements —The Company categorizes its financial assets and liabilities measured and reported at fair value in the financial statements on a recurring basis based upon the level of judgments associated with the inputs used to measure their fair value. Hierarchical levels, which are directly related to the amount of subjectivity associated with the inputs used to determine the fair value of financial assets and liabilities, are as follows:

- Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

2. Summary of Significant Accounting Policies (Continued)

- Level 2—Inputs (other than quoted prices included in Level 1) are either directly or indirectly observable for the assets or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.
- Level 3—Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

Each major category of financial assets and liabilities measured at fair value on a recurring basis are categorized based upon the lowest level of significant input to the valuations. The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. Financial instruments in Level 1 generally include US treasuries and mutual funds listed in active markets.

The Company's only assets and liabilities which were measured at fair value as of December 31, 2015 and December 31, 2014 were its cash and cash equivalents of $282.9 million and $159.2 million, respectively. These amounts were measured at Level 1 using quoted prices in active markets for identical assets at the measurement date. The Company's cash and cash equivalents permit daily redemption and the fair values of these investments are based upon the quoted prices in active markets provided by the holding financial institutions. Cash equivalents consist of liquid investments with a maturity of three months or less from the date of purchase and the short-term investments consist of instruments with maturities greater than three months.

The Company recognizes transfers between levels within the fair value hierarchy, if any, at the end of each quarter. There were no transfers in or out of Level 1, Level 2 or Level 3 during 2015 and 2014.

As of December 31, 2015 and 2014, the Company held no securities that were in an unrealized loss or gain position.

The Company reviews the status of each security quarterly to determine whether an other-than-temporary impairment has occurred. In making its determination, the Company considers a number of factors, including: (1) the significance of the decline, (2) whether the securities were rated below investment grade, (3) how long the securities have been in an unrealized loss position, and (4) the Company's ability and intent to retain the investment for a sufficient period of time for it to recover.

Foreign currency —The Company has operations in the United States, Ireland, Germany, France, the United Kingdom and the Netherlands. The results of its non-US dollar based functional currency operations are translated to US dollars at the average exchange rates during the period. Assets and liabilities are translated at the exchange rate prevailing at the balance sheet date. Equity is translated at the prevailing exchange rate at the date of the equity transaction. Translation adjustments, when material, will be reflected in shareholders' equity and included as a component of other comprehensive loss.

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

2. Summary of Significant Accounting Policies (Continued)

The Company realizes foreign currency transaction gains/(losses) in the normal course of business based on movements in the applicable exchange rates. These gains/(losses) are included as a component of other (expense) / income, net.

Concentration of Credit Risk —Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and cash equivalents. The Company places its cash equivalents with high credit-quality financial institutions and may invest its short- term investments in US treasury securities, mutual funds and government agency bonds. The Company has established guidelines relative to credit ratings and maturities that seek to maintain safety and liquidity.

The Company sources its raw materials from single suppliers. In addition, the production of the Company's lead product candidate, ARIKAYCE, is currently performed by a sole manufacturer. The Company entered into a contract manufacturing agreement with a second manufacturer to construct a production area for ARIKAYCE which was substantially completed in 2015. This second site will eventually supply ARIKAYCE at the larger scales necessary to support commercialization. The inability of the suppliers or manufacturers to fulfill supply requirements of the Company could materially impact future operating results. A change in the relationship with the suppliers or manufacturer, or an adverse change in their business, could materially impact future operating results.

Revenue Recognition —In 2015, the French National Agency for Medicines and Health Products Safety (ANSM) granted LAI a Temporary Authorization for Use (Autorisation Temporaire d'Utilisation or ATU). Pursuant to this program, the Company shipped product to pharmacies after receiving requests from physicians for patients in France. For the year ended December 31, 2015, the revenue recorded was immaterial and is included as a component of "other income." The Company is initiating expanded access programs (EAPs) in other select territories in Europe, some of which may be fully reimbursed. EAPs are intended to make products available on a named patient basis before they are commercially available in accordance with local regulations. The Company did not recognize any revenue in 2014. In 2013, the Company's other revenue solely consists of an $11.5 million payment received from Premacure (now Shire plc) in exchange for the Company's right to receive royalties under its license agreement with Premacure. The Company recorded this as other revenue after all four revenue recognition criteria were present and the Company had no continuing performance obligations related to the payment received.

The Company recognizes revenues when all of the following four criteria are present: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed or determinable; and collectability is reasonably assured.

Where the Company has continuing performance obligations under the terms of a collaborative arrangement, non-refundable upfront license payments received upon contract signing are recorded as deferred revenue and recognized as revenue as the related activities are performed. The period over which these activities are to be performed is based upon management's estimate of the development period. Changes in management's estimate could change the period over which revenue is recognized. Research and/or development payments are recognized as revenues as the related research and/or development activities are performed and when the Company has no continuing performance obligations related to the research and development payment received.

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

2. Summary of Significant Accounting Policies (Continued)

Where the Company has no continuing involvement under a collaborative arrangement, the Company records nonrefundable license fee revenues when the Company has the contractual right to receive the payment, in accordance with the terms of the collaboration agreement, and records milestones upon appropriate notification to the Company of achievement of the milestones by the collaborative partner.

The Company recognizes revenue from milestone payments when earned, provided that (i) the milestone event is substantive and its achievability was not reasonably assured at the inception of the agreement and (ii) the Company does not have ongoing performance obligations related to the achievement of the milestone earned. Milestone payments are considered substantive if all of the following conditions are met: the milestone payment (a) is commensurate with either the vendor's performance to achieve the milestone or the enhancement of the value of the delivered item or items as a result of a specific outcome resulting from the vendor's performance to achieve the milestone, (b) relates solely to past performance, and (c) is reasonable relative to all of the deliverables and payment terms (including other potential milestone consideration) within the arrangement. Any amounts received under the agreement in advance of performance, if deemed substantive, are recorded as deferred revenue and recognized as revenue as the Company completes its performance obligations.

With regard to recognizing revenue for multiple deliverable revenue arrangements, each deliverable within a multiple-deliverable revenue arrangement is accounted for as a separate unit of accounting if both of the following criteria are met: (1) the delivered item or items have value to the customer on a standalone basis and (2) for an arrangement that includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in the Company's control.

In addition, multiple deliverable revenue arrangement consideration is allocated at the inception of an arrangement to all deliverables using the relative selling price method. The Company also applies a selling price hierarchy for determining the selling price of a deliverable, which includes (1) vendor-specific objective evidence, if available, (2) third-party evidence, if vendor-specific objective evidence is not available, and (3) estimated selling price if neither vendor-specific nor third-party evidence is available.

Deferred revenue associated with a non-refundable payment received under a collaborative agreement that is terminated prior to its completion results in an immediate recognition of the deferred revenue.

Research and Development —Research and development expenses consist primarily of salaries, benefits and other related costs, including stock based compensation, for personnel serving in the Company's research and development functions, and other internal operating expenses, the cost of manufacturing a drug candidate, including the medical devices for drug delivery, for clinical study, the cost of conducting clinical studies, and the cost of conducting preclinical and research activities. The Company's expenses related to manufacturing its drug candidate and medical devices for clinical study are primarily related to activities at contract manufacturing organizations that manufacture ARIKAYCE, INS1009 and the medical devices for the Company's use. The Company's expenses related to clinical trials are primarily related to activities at contract research organizations that conduct and

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

2. Summary of Significant Accounting Policies (Continued)

manage clinical trials on the Company's behalf. These contracts set forth the scope of work to be completed at a fixed fee or amount per patient enrolled. Payments under these contracts primarily depend on performance criteria such as the successful enrollment of patients or the completion of clinical trial milestones as well as time-based fees. Expenses are accrued based on contracted amounts applied to the level of patient enrollment and to activity according to the clinical trial protocol. Nonrefundable advance payments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are then recognized as an expense as the related goods are delivered or the services are performed, or when the goods or services are no longer expected to be provided.

Stock-Based Compensation —The Company recognizes stock-based compensation expense for awards of equity instruments to employees and directors based on the grant-date fair value of those awards. The grant-date fair value of the award is recognized as compensation expense ratably over the requisite service period, which generally equals the vesting period of the award, and if applicable, is adjusted for expected forfeitures. The Company also grants performance-based stock options to employees. The grant-date fair value of the performance-based stock options is recognized as compensation expense over the implicit service period using the accelerated attribution method once it is probable that the performance condition will be achieved. Stock-based compensation expense is included in both research and development expenses and general and administrative expenses in the Consolidated Statements of Comprehensive Loss.

Certain awards deemed to be granted outside of the Company's equity incentive plans require the Company to use liability accounting. These awards are classified as a liability and are remeasured at fair value at the end of each reporting period until such time they are deemed to be granted under the Company's equity incentive plans. Changes in fair value are included in compensation expense in the Consolidated Statements of Comprehensive Loss (see additional disclosures related to awards granted outside of the 2000 Stock Incentive Plan in Note 8, Stock-Based Compensation).

Income Taxes —The Company accounts for income taxes under the asset and liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and operating loss carry forwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date.

A valuation allowance is recorded to reduce the deferred tax assets to the amount that is expected to be realized. In evaluating the need for a valuation allowance, the Company takes into account various factors, including the expected level of future taxable income and available tax planning strategies. If actual results differ from the assumptions made in the evaluation of a valuation allowance, the Company records a change in valuation allowance through income tax expense in the period such determination is made.

The Company uses a comprehensive model for how it measures, presents and discloses an uncertain tax position taken or expected to be taken in a tax return. The Company may recognize the

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

2. Summary of Significant Accounting Policies (Continued)

tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by taxing authorities, based solely on the technical merits of the position. The tax benefits recognized in the financial statements from such a position should be measured based on the largest benefit that has a greater than 50% likelihood to be sustained upon ultimate settlement. The Company has no uncertain tax positions as of December 31, 2015 that qualify for either recognition or disclosure in the consolidated financial statements.

The Company's policy for interest and penalties related to income tax exposures is to recognize interest and penalties as a component of the income taxes on continuing operations in the Consolidated Statements of Comprehensive Loss.

Net Loss Per Common Share —Basic net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding during the period. Diluted net loss per common share is computed by dividing net loss by the weighted average number of common shares and other dilutive securities outstanding during the period. Potentially dilutive securities from stock options, restricted stock units and warrants to purchase common stock would be antidilutive as the Company incurred a net loss in all periods presented. Potentially dilutive common shares resulting from the assumed exercise of outstanding stock options and warrants are determined based on the treasury stock method.

The following table sets forth the reconciliation of the weighted average number of shares used to compute basic and diluted net loss per share for the years ended December 31, 2015, 2014 and 2013.

	Years Ended December 31,		
	2015	2014	2013
	(In thousands, except per share amounts)		
Numerator:			
Net loss:	$ (118,183)	$ (79,159)	$ (56,073)
Denominator:			
Weighted average common shares used in calculation of basic net loss per share:	58,633	43,095	34,980
Effect of dilutive securities:			
Common stock options	-	-	-
Restricted stock and restricted stock units	-	-	-
Common stock warrant	-	-	-
Weighted average common shares outstanding used in calculation of diluted net loss per share	58,633	43,095	34,980
Net loss per share:			
Basic and Diluted	$ (2.02)	$ (1.84)	$ (1.60)

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

2. Summary of Significant Accounting Policies (Continued)

The following potentially dilutive securities have been excluded from the computations of diluted weighted-average common shares outstanding as of December 31, 2015, 2014 and 2013 as their effect would have been anti-dilutive (in thousands).

	2015	2014	2013
Stock options to purchase common stock	5,274	4,400	3,633
Restricted stock and restricted stock units	44	21	93

Segment Information —The Company currently operates in one business segment, which is the development and commercialization of inhaled therapies for patients with serious lung diseases. A single management team that reports to the Chief Executive Officer comprehensively manages the entire business. The Company does not operate separate lines of business with respect to its products or product candidates. Accordingly, the Company does not have separate reportable segments.

New Accounting Pronouncements —In April 2015, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2015-03, Simplifying the Presentation of Debt Issuance Costs. The new standard requires that debt issuance costs be presented in the balance sheet as a direct reduction from the carrying value of the associated debt liability, consistent with the presentation of a debt discount. The standard is effective for public entities for annual and interim periods beginning after December 15, 2015. Early adoption is permitted for financial statements that have not been previously issued. The new guidance will be applied on a retrospective basis. The Company has determined the impact of this standard will be not be material on its consolidated results of operations and financial position.

In November 2015, the FASB issued ASU 2015-17, Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes, which updated and simplified the presentation of deferred income taxes. Current generally accepted accounting principles require an entity to separate deferred income tax liabilities and assets into current and noncurrent amounts in a classified statement of financial position. To simplify the presentation of deferred income taxes, the amendments in this update require that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position. The current requirement that deferred tax assets and liabilities of a tax-paying component of an entity be offset and presented as a single amount is not affected by the amendments in this update. The amendments in this update are effective for financial statements issued for annual periods beginning after December 15, 2016 and interim periods within those annual periods. Earlier application is permitted as of the beginning of an interim or annual reporting period. The Company has early adopted the update effective with its annual reporting period ended December 31, 2015. The adoption of this update did not have a significant impact on the Company's consolidated financial statements.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

3. Accrued Expenses

Accrued expenses consist of the following:

	As of December 31,	
	2015	2014
	(in thousands)	
Accrued clinical trial expenses	$ 4,331	$ 2,113
Accrued compensation	4,302	4,317
Accrued professional fees	1,202	542
Accrued technical operation expenses	702	762
Accrued interest payable	199	258
Accrued construction costs	57	1,500
Other accrued expenses	202	146
	$ 10,995	$ 9,638

4. Identifiable Intangible Assets

The Company's only identifiable intangible asset was in-process research and development ("IPRD") related to ARIKAYCE as of December 31, 2015 and 2014. The total intangible IPRD asset was $58.2 million as of December 31, 2015 and 2014, which resulted from the initial amount recorded at the time of the Company's merger with Transave in 2010 and subsequent adjustments in the value. Historically, the Company uses the income approach to derive the fair value of in-process research and development assets. This approach calculates fair value by estimating future cash flows attributable to the assets and then discounting these cash flows to a present value using a risk-adjusted discount rate. Identifiable intangible assets are measured at their respective fair values and are not amortized until commercialization. Once commercialization occurs, intangible assets will be amortized over their estimated useful lives. The Company did not identify any indicators of impairment of its in-process research and development intangible assets as of December 31, 2015.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

5. Fixed Assets, net

Fixed assets are stated at cost and depreciated or amortized using the straight-line method, based on useful lives as follows:

Asset Description	Estimated Useful Life (years)	As of December 31, 2015	As of December 31, 2014
		(in thousands)	
Lab equipment	7	$ 3,957	$ 3,449
Furniture and fixtures	7	1,127	1,127
Computer hardware and software	3 - 5	1,969	921
Office equipment	7	65	65
Manufacturing Equipment	7	980	669
Leasehold improvements	lease term	5,300	4,627
		13,398	10,858
Less accumulated depreciation		(5,306)	(3,324)
Fixed assets, net		$ 8,092	$ 7,534

Depreciation expense was $2.0 million, $1.1 million and $0.7 million for the years ended December 31, 2015, 2014 and 2013, respectively. Depreciation expense includes depreciation for equipment under capital lease obligations.

6. Debt

On June 29, 2012, the Company and its domestic subsidiaries, as co-borrowers, entered into a Loan and Security Agreement with Hercules Technology Growth Capital, Inc. ("Hercules") that allowed the Company to borrow up to $20.0 million ("Loan Agreement") at an interest rate of 9.25%. On December 15, 2014, Company and Hercules entered into a third amendment (the "Third Amendment") to the Loan Agreement. In connection with the Third Amendment, the Company paid a commitment fee of $25,000, and at the closing, paid a facility fee of $125,000. Under the Third Amendment, the amount of borrowings was increased by $5.0 million to an aggregate total of $25.0 million and the interest-only period was extended through December 31, 2015. In December 2015, the Company entered into a fifth amendment to the Loan Agreement, to exercise an option to extend the maturity date to January 1, 2018 with a payment to Hercules of $250,000. The amendment extends the interest-only period, with principal repayments beginning in October 2016.

In connection with the Loan Agreement, the Company granted the lender a first position lien on all of the Company's assets, excluding intellectual property. Prepayment of the loans made pursuant to the Loan Agreement is subject to penalty and the Company is required to pay an "end of term" charge of $390,000, which is being charged to interest expense (and accreted to the debt) using the effective interest method over the life of the Loan Agreement. The end of term fee was paid in full as required in January 2016. Debt issuance fees paid to the lender were recorded as a discount on the

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

6. Debt (Continued)

debt and are being amortized to interest expense using the effective interest method over the life of the Loan Agreement. Debt issuance fees paid to third parties were capitalized and are being amortized to interest expense using the effective interest method over the life of the Loan Agreement.

The Loan Agreement also contains representations and warranties by us and the lender and indemnification provisions in favor of the lender and customary covenants (including limitations on other indebtedness, liens, acquisitions, investments and dividends, but no financial covenants), and events of default (including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of the lender's security interest or in the collateral, and events relating to bankruptcy or insolvency). Upon the occurrence of an event of default, a default interest rate of an additional 5% may be applied to the outstanding loan balances, and the lender may terminate its lending commitment, declare all outstanding obligations immediately due and payable, and take such other actions as set forth in the Loan Agreement. In addition, pursuant to the Loan Agreement, the lender has the right to participate, in an amount of up to $1.0 million, in certain future private equity financing(s) by the Company.

In conjunction with entering into the original Loan Agreement in 2012, the Company granted a warrant to the lender to purchase shares of the Company's common stock. Since the warrant was granted in conjunction with entering into the Loan Agreement, the relative fair value of the warrant was recorded as equity and debt discount. On April 30, 2013, the lender exercised the warrant in full. The debt discount is being amortized to interest expense over the term of the related debt using the effective interest method.

The following table presents the components of the Company's debt balance as of December 31, 2015:

	December 31, 2015 (in thousands)
Debt:	
Notes payable	$ 25,000
Accretion of end of term charge	390
Issuance fees paid to lender	(250)
Current portion of long-term debt	(3,113)
Long-term debt	$ 22,027

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

6. Debt (Continued)

Future principal repayments of the Company's long-term debt are as follows (in thousands):

Year Ending in December 31:		
2016	$	2,873
2017		12,180
2018 (due on January 1, 2018)		9,947
	$	25,000

The estimated fair value of the debt (categorized as a Level 2 liability for fair value measurement purposes) is determined using current market factors and the ability of the Company to obtain debt at comparable terms to those that are currently in place. As of December 31, 2015 and 2014, the fair value of the Company's debt approximates the carrying amount.

7. Stockholders' Equity

Common Stock —As of December 31, 2015, the Company had 500,000,000 shares of common stock authorized with a par value of $0.01 and 61,813,995 shares of common stock issued and outstanding. In addition, as of December 31, 2015, the Company had reserved 5,273,722 shares of common stock for issuance upon the exercise of outstanding common stock options and 43,554 shares of common stock for issuance upon the vesting of restricted stock units.

On December 15, 2014, in connection with the Third Amendment to the Loan Agreement, the Company entered into a stock purchase agreement with Hercules pursuant to which the Company issued 70,771 shares of its common stock, at a price of $14.13 per share (the closing price of the Company's common stock as reported by the NASDAQ Stock Market on December 12, 2014), for an aggregate purchase price of approximately $1.0 million. The securities sold in this private placement have not been registered under the Securities Act of 1933, as amended (the "Act") and may not be offered or sold in the United States in the absence of an effective registration statement or exemption from the registration requirements under the Act. The issuance of the securities in this transaction were exempt from registration under Section 4(2) of the Securities Act of 1933.

On April 6, 2015, the Company completed an underwritten public offering of 11,500,000 shares of the Company's common stock, which included the underwriter's exercise in full of its over-allotment option of 1,500,000 shares, at a price to the public of $20.65 per share. The Company's net proceeds from the sale of the shares, after deducting the underwriter's discount and offering expenses of $14.5 million, were $222.9 million.

On August 18, 2014, the Company completed an underwritten public offering of 10,235,000 shares of the Company's common stock, which included the underwriter's exercise in full of its over-allotment option of 1,335,000 shares, at a price to the public of $11.25 per share. The Company's net proceeds from the sale of the shares, after deducting the underwriter's discount and offering expenses of $7.1 million, were $108.0 million.

On July 22, 2013, the Company completed an underwritten public offering of 6,900,000 shares of the Company's common stock, which included the underwriter's exercise in full of its over-allotment

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

7. Stockholders' Equity (Continued)

option of 900,000 shares, at a price to the public of $10.40 per share. The Company's net proceeds from the sale of the shares, after deducting the underwriter's discount and offering expenses of $4.7 million, were $67.0 million.

Preferred Stock —As of December 31, 2015 and 2014, the Company had 200,000,000 shares of preferred stock authorized with a par value of $0.01 and no shares of preferred stock were issued and outstanding.

Warrant —In conjunction with entering into the Loan Agreement in 2012 (See Note 6—Debt), the Company granted a warrant to the lender to purchase 329,932 shares of the Company's common stock at an exercise price of $2.94 per share. The fair value of the warrant of $0.8 million was calculated using the Black-Scholes warrant-pricing methodology at the date of issuance and was recorded as equity and as a discount to the debt and was amortized to interest expense over the term of the related debt using the effective interest method. On April 30, 2013, the lender exercised the warrant in full via the "net issuance" method specified in the warrant agreement. In accordance with such provisions, the Company issued and delivered 223,431 shares of common shares to the lender on May 1, 2013. As a result of the exercise, the warrant is no longer outstanding and there are no additional shares issuable under this instrument.

8. Stock-Based Compensation

The Company's current equity compensation plan, the 2015 Incentive Plan, was approved by shareholders at the Company's Annual Meeting of Shareholders on May 21, 2015. The 2015 Incentive Plan is administered by the Compensation Committee and the Board of Directors of the Company. Under the terms of the 2015 Incentive Plan, the Company is authorized to grant a variety of incentive awards based on its common stock, including stock options (both incentive stock options and non-qualified stock options), performance options/shares and other stock awards, as well as the payment of incentive bonuses to all employees and non-employee directors. On May 21, 2015, 5,000,000 shares of the Company's common stock were authorized and as of December 31, 2015, there were 4,295,221 shares remaining for future grants (or issuances) of stock options, stock appreciation rights, restricted stock, restricted stock units and incentive bonuses under the 2015 Incentive Plan. The 2015 Incentive Plan will terminate on April 9, 2025 unless it is extended or terminated earlier pursuant to its terms. In addition, from time to time, the Company makes inducement grants of stock options. These awards are made pursuant to the NASDAQ inducement grant exception as a component of new hires' employment compensation in connection with the Company's equity grant program. During the year ended December 31, 2015, the Company granted 227,000 inducement stock options to new employees.

During 2013, the Company had three equity compensation plans: the 2013 Incentive Plan, the Amended and Restated 2000 Stock Incentive Plan, as amended (the "2000 Stock Incentive Plan") and the Amended and Restated 2000 Employee Stock Purchase Plan (the "Stock Purchase Plan"). Both the 2000 Stock Incentive Plan and the Stock Purchase Plan were adopted by the Company's Board of Directors in 2000. Upon the approval of the 2013 Incentive Plan, no additional awards were issued under the 2000 Stock Incentive Plan and the shares remaining for future grant under the 2000 Stock Incentive Plan were transferred to the 2013 Incentive Plan.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

8. Stock-Based Compensation (Continued)

During the first quarter of 2013, the Company completed a review of equity compensation awards granted under its 2000 Stock Incentive Plan and determined that it had inadvertently exceeded the annual per-person sub-limits involving certain awards previously made to certain of its current and past officers and directors (the "excess awards"). The aggregate amount of common stock represented by these excess awards, which consisted of RSUs and stock options, was approximately 1.4 million shares. These awards were deemed to be granted outside of the 2000 Stock Incentive Plan and as such the Company applied liability accounting to these awards. On May 23, 2013 (the date of the Company's 2013 Annual Meeting of Stockholders), shareholders approved the grants associated with the excess awards, which as of this date, allowed the excess awards to be deemed granted under the 2000 Stock Incentive Plan. As a result, the excess awards were re-measured at fair value on May 23, 2013 and the liability was reclassified to additional paid-in capital. The unrecognized fair value calculated for the excess awards as of May 23, 2013 is being recognized as compensation expense ratably over the remaining requisite service period for each award.

Stock Options —The Company calculates the fair value of stock options granted using the Black-Scholes valuation model. The Company calculated the fair value of stock options granted outside of the 2000 Stock Incentive Plan using liability accounting. These awards were classified as a liability and were re-measured at fair value at the end of each reporting period using the Black-Scholes valuation model and changes in fair value were included in compensation expense in the Consolidated Statements of Comprehensive Loss (see additional disclosures related to stock options granted outside the 2000 Stock Incentive Plan at the end of this footnote).

The following table summarizes the grant date fair value and assumptions used in determining the fair value of all stock options granted, including grants of inducement shares, during the years ended December 31, 2015, 2014 and 2013.

	2015	2014	2013
Volatility	78% - 82%	83% - 86%	86% - 96%
Risk-free interest rate	1.31% - 1.75%	1.46% - 1.83%	0.65% - 1.65%
Dividend yield	0.0%	0.0%	0.0%
Expected option term (in years)	6.25	6.25	6.25
Weighted-average fair value of stock options granted	$14.20	$11.74	$8.16

For the years ended December 31, 2015, 2014 and 2013, the volatility factor was based on the Company's historical volatility since the closing of the Merger on December 1, 2010. The expected life was determined using the simplified method as described in ASC Topic 718, "Accounting for Stock Compensation", which is the midpoint between the vesting date and the end of the contractual term. The risk-free interest rate was based on the US Treasury yield in effect at the date of grant. Forfeitures are based on actual percentage of option forfeitures since the closing of the Merger on December 1, 2010, and this is the basis for future forfeiture expectations.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

8. Stock-Based Compensation (Continued)

From time to time, the Company grants performance-condition options to certain employees. Vesting of these options is subject to the Company achieving certain performance criteria established at the date of grant and the individuals fulfilling a service condition (continued employment). As of December 31, 2015, the Company had performance options totaling 158,334 shares outstanding. As a result of the Marketing Authorization Application ("MAA") acceptance for ARIKAYCE, which was received from the European Medicines Agency ("EMA") in February 2015, performance options totaling $1.5 million were recorded as non-cash compensation expense in the first quarter of 2015.

The following table summarizes stock option activity for stock options granted under the 2013 Incentive Plan and the 2000 Stock Incentive Plan, as well as grants of inducement shares, for the years ended December 31, 2015, 2014 and 2013 as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in '000)
Options outstanding at January 1, 2013	1,817,839	$ 4.10		
Granted	2,323,500	10.53		
Exercised	(371,743)	4.37		
Forfeited and expired	(136,600)	10.49		
Options outstanding at December 31, 2013	3,632,996	7.94		
Vested and expected to vest at December 31, 2013	3,402,306	7.88		
Exercisable at December 31, 2013	484,213	4.25		
Options outstanding at December 31, 2013	3,632,996	$ 7.94		
Granted	1,600,452	16.10		
Exercised	(283,057)	6.11		
Forfeited and expired	(550,285)	11.42		
Options outstanding at December 31, 2014	4,400,106	10.59		
Vested and expected to vest at December 31, 2014	3,891,511	10.32		
Exercisable at December 31, 2014	1,235,710	6.90		
Options outstanding at December 31, 2014	4,400,106	$ 10.59		
Granted	1,902,850	20.45		
Exercised	(481,140)	10.62		
Forfeited and expired	(548,094)	15.43		
Options outstanding at December 31, 2015	5,273,722	13.64	8.00	$ 29,699
Vested and expected to vest at December 31, 2015	5,059,645	13.46	7.96	$ 29,240
Exercisable at December 31, 2015	1,991,141	8.70	7.11	$ 19,128

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

8. Stock-Based Compensation (Continued)

The total intrinsic value of stock options exercised during the years ended December 31, 2015, 2014 and 2013 was $4.7 million, $2.5 million and $2.7 million, respectively.

As of December 31, 2015, there was $26.9 million of unrecognized compensation expense related to unvested stock options, which is expected to be recognized over a weighted average period of 2.5 years. Included above in unrecognized compensation expense was $1.2 million related to outstanding performance-based options. The following table summarizes the range of exercise prices and the number of stock options outstanding and exercisable as of December 31, 2015:

Outstanding as of December 31, 2015					Exercisable as of December 31, 2015	
Range of Exercise Prices		Number of Options	Weighted Average Remaining Contractual Term (in years)	Weighted Average Exercise Price	Number of Options	Weighted Average Exercise Price
$ 3.03	$ 3.29	153,878	5.62	$ 3.05	152,017	$ 3.05
$ 3.40	$ 3.40	708,314	6.69	$ 3.40	531,236	$ 3.40
$ 3.60	$ 6.90	583,542	6.90	$ 6.01	389,433	$ 5.90
$ 6.96	$ 12.44	693,090	7.37	$ 11.36	378,156	$ 11.35
$ 12.58	$ 14.20	527,974	8.36	$ 12.78	189,989	$ 12.76
$ 14.24	$ 16.07	768,900	8.48	$ 15.36	161,331	$ 14.46
$ 16.09	$ 20.49	782,624	8.46	$ 19.28	183,354	$ 19.52
$ 20.92	$ 22.14	106,300	9.14	$ 21.54	5,625	$ 21.54
$ 22.76	$ 22.76	793,000	9.38	$ 22.76	-	-
$ 22.84	$ 27.38	156,100	9.41	$ 23.76	-	-

Restricted Stock and Restricted Stock Units —The Company may grant Restricted Stock ("RS") and Restricted Stock Units ("RSUs") to employees and non-employee directors. Each RS and RSU represents a right to receive one share of the Company's common stock upon the completion of a specific period of continued service or achievement of a certain milestone. RS and RSU awards granted are valued at the market price of the Company's common stock on the date of grant. The Company recognizes noncash compensation expense for the fair values of these RS and RSUs on a straight-line basis over the requisite service period of these awards.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

8. Stock-Based Compensation (Continued)

The following table summarizes RSU awards granted during the years ended December 31, 2015, 2014 and 2013:

	Number of RSU's	Weighted Average Grant Price
Outstanding at January 1, 2013	215,525	$ 6.26
Granted	55,317	6.77
Released	(177,316)	6.42
Forfeited	(885)	5.00
Outstanding at December 31, 2013	92,641	$ 6.27
Granted	20,502	19.47
Released	(92,641)	6.27
Forfeited	-	-
Outstanding at December 31, 2014	20,502	$ 19.47
Granted	49,776	16.07
Released	(26,724)	18.68
Forfeited	-	-
Outstanding at December 31, 2015	43,554	$ 16.07
Expected to Vest	43,554	$ 16.07

Awards Granted Outside of the 2000 Stock Incentive Plan —As described above, during the first quarter of 2013, the Company completed a review of equity compensation awards granted under its 2000 Stock Incentive Plan and determined that it had inadvertently exceeded the annual per-person sub-limits involving certain awards previously made to certain of its current and past officers and directors (the "excess awards"). The aggregate amount of common stock represented by these excess awards, which consisted of RSUs and stock options, was approximately 1.4 million shares. These awards were deemed to be granted outside of the 2000 Stock Incentive Plan and as such the Company applied liability accounting to these awards. On May 23, 2013 (the date of the Company's 2013 Annual Meeting of Stockholders), shareholders approved the grants associated with the excess awards, which as of this date, allowed the excess awards to be deemed granted under the 2000 Stock Incentive Plan. As a result, the excess awards were re-measured at fair value on May 23, 2013 and the liability was reclassified to additional paid-in capital. The unrecognized fair value calculated for the excess awards as of May 23, 2013 is being recognized as compensation expense ratably over the remaining requisite service period for each award.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

8. Stock-Based Compensation (Continued)

The following table summarizes the stock-based compensation recorded in the Consolidated Statements of Comprehensive Loss related to stock options and RSUs during the years ended December 31, 2015, 2014 and 2013:

	2015	2014	2013
		(in millions)	
Research and development expenses	$ 4.0	$ 4.5	$ 2.4
General and administrative expenses	11.6	6.8	6.3
Total(1)	$ 15.6	$ 11.3	$ 8.7

(1) Includes $2.3 million, $2.4 million and $4.1 million for the years ended December 31, 2015, 2014 and 2013, respectively, for the remeasurement of certain stock options and RSUs that occurred during May 2013.

9. Income Taxes

The benefit for income taxes was $2.0 million, $10.4 million and $1.2 million and the effective rates were approximately 2%, 12% and 2% for the years ended December 31, 2015, 2014 and 2013, respectively. The benefit for income taxes recorded and the effective tax rates for the year ended December 31, 2015, 2014 and 2013 primarily reflect the reversal of valuation allowances previously recorded against the Company's New Jersey State net operating losses ("NOL") that resulted from the Company's sale of $24.3 million, $110.5 million and $27.0 million of its New Jersey State NOLs under the State of New Jersey's Technology Business Tax Certificate Transfer Program (the "Program") for cash of $2.0 million, $10.4 million and $1.2 million, respectively, net of commissions. The Program allows qualified technology and biotechnology businesses in New Jersey to sell unused amounts of NOLs and defined research and development tax credits for cash. In 2015, the Company reached the lifetime maximum cap of NOLs that can be sold to the State of New Jersey. Therefore the Company will no longer receive cash proceeds from this program in the future.

The Company is subject to US federal and state income taxes and the statute of limitations for tax audit is open for the federal tax returns for the years ended 2012 and later, and is generally open for certain states for the years 2011 and later. The Company's US federal tax return for the year ended December 31, 2013 is currently under audit by the Internal Revenue Service. The Company has incurred net operating losses since inception, except for the year ended December 31, 2009. Such loss carryforwards would be subject to audit in any tax year in which those losses are utilized, notwithstanding the year of origin.

The Company's policy is to recognize interest accrued related to unrecognized tax benefits and penalties in income tax expense. The Company has recorded no such expense. As of December 31, 2015 and 2014, the Company has recorded no reserves for unrecognized income tax benefits, nor has it recorded any accrued interest or penalties related to uncertain tax positions. The Company does not

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

9. Income Taxes (Continued)

anticipate any material changes in the amount of unrecognized tax positions over the next twelve months.

For the year ended December 31, 2015, the Company was also subject to foreign income taxes as a result of new legal entities established for activities in Europe. The Company's loss before income taxes was generated in the US and globally as follows (in thousands):

	Years ended December 31,		
	2015	2014	2013
US	$ (100,278)	$ (89,581)	$ (57,294)
Foreign	(19,876)	-	-
Total	$ (120,154)	$ (89,581)	$ (57,294)

The Company's income tax provision / (benefit) consisted of the following (in thousands):

	Years ended December 31,		
	2015	2014	2013
Current:			
Federal	$ -	$ -	$ -
State	(2,015)	(10,422)	(1,221)
Foreign	44	-	-
	(1,971)	(10,422)	(1,221)
Deferred:			
Federal	-	-	-
State	-	-	-
Foreign	-	-	-
	-	-	-
Total	$ (1,971)	$ (10,422)	$ (1,221)

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

9. Income Taxes (Continued)

The reconciliation between the federal statutory tax rate of 34% and the Company's effective tax rate is as follows:

	Years Ended December 31,		
	2015	**2014**	**2013**
Statutory federal tax rate	34%	34%	34%
Permanent items	(4)%	(3)%	0%
State income taxes, net of federal benefit	4%	(7)%	7%
R&D and other tax credits	12%	5%	7%
Foreign income taxes	(1)%	0%	0%
Change in state tax rate	0%	0%	2%
Change in valuation allowance	(43)%	(17)%	(49)%
Other	0%	0%	1%
Effective tax rate	2%	12%	2%

Deferred tax assets and liabilities are determined based on the difference between financial statement and tax bases using enacted tax rates in effect for the year in which the differences are expected to reverse. The components of the deferred tax assets and liabilities consist of the following:

	As of December 31,	
	2015	**2014**
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 195,052	$ 160,758
General business credits	33,360	18,150
Alternative minimum tax (AMT) credit	418	418
Other	10,569	7,863
Gross deferred tax assets	$ 239,399	$ 187,189
Deferred tax liabilities:		
In-process research and development	$ (23,245)	$ (23,245)
Deferred tax liabilities	$ (23,245)	$ (23,245)
Net deferred tax assets	$ 216,154	$ 163,944
Valuation allowance	(216,154)	(163,944)
Net deferred tax assets	$ -	$ -

The net deferred tax assets (prior to applying the valuation allowance) of $216.2 million and $163.9 million at December 31, 2015 and 2014, respectively, primarily consist of net operating loss carryforwards for income tax purposes. Due to the Company's history of operating losses, the Company recorded a full valuation allowance on its net deferred tax assets by increasing the valuation allowance by $52.3 million and $15.8 million in 2015 and 2014, respectively, as it is more likely than not that such tax benefits will not be realized.

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

9. Income Taxes (Continued)

At December 31, 2015, the Company had federal net operating loss carryforwards for income tax purposes of approximately $538.7 million. Due to the limitation on NOLs as more fully discussed below, $360.4 million of the NOLs are available to offset future taxable income, if any. The NOL carryovers and general business tax credits expire in various years beginning in 2018. For state tax purposes, the Company has approximately $115.9 million of New Jersey NOLs available to offset against future taxable income or to be sold as part of the New Jersey Transfer Program. The Company also has California and Virginia NOLs that are entirely limited due to Section 382 (as discussed below), in addition to changing state apportionment allocations, as the Company is now 100% resident in New Jersey.

During 2014, the Company completed an Internal Revenue Code Section 382 ("Section 382") analysis in order to determine the amount of losses that are currently available for potential offset against future taxable income, if any. It was determined that the utilization of the Company's NOL and general business tax credit carryforwards generated in tax periods up to and including December 2010 (the "December 2010 and prior NOLs") were subject to substantial limitations under Section 382 due to ownership changes that occurred at various points from the Company's original organization through December 2010. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period. Since the Company's formation, it has raised capital through the issuance of common stock on several occasions which, combined with the purchasing shareholders' subsequent disposition of those shares, resulted in multiple changes in ownership, as defined by Section 382 since the Company's formation in 1999. These ownership changes resulted in substantial limitations on the use of the Company's NOLs and general business tax credit carryforwards up to and including December 2010. The Company continues to track all of its NOLs and tax credit carryforwards but has provided a full valuation allowance to offset those amounts.

10. License and Collaboration Agreements

In-License Agreements

PARI Pharma GmbH —In April 2008, the Company entered into a licensing agreement with PARI Pharma GmbH ("PARI") for use of the optimized eFlow Nebulizer System for delivery of ARIKAYCE in treating patients with NTM infections, CF and bronchiectasis. The Company has rights to several US and foreign issued patents and patent applications involving improvements to the optimized eFlow Nebulizer System. Under the licensing agreement, PARI is entitled to receive payments either in cash, qualified stock or a combination of both, at PARI's discretion, based on achievement of certain future milestone events including first acceptance of MAA submission (or equivalent) in the US of ARIKAYCE and the device, first receipt of marketing approval in the US for ARIKAYCE and the device, and first receipt of marketing approval in a major EU country for ARIKAYCE and the device. In addition, PARI is entitled to receive royalty payments in the mid-single digits on commercial net sales of ARIKAYCE, subject to certain specified annual minimum royalties. See below for information related to the commercialization agreement with PARI.

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

10. License and Collaboration Agreements (Continued)

Respironics —In November 2015, the Company entered into an agreement with Respironics Inc., a division of Philips (Respironics), for the clinical supply of devices to be used in the development of INS1009 for PAH. The agreement calls for payments to Respironics upon the achievement of certain clinical milestones relating to the development of INS1009 aggregating $7.6 million. In addition, the Company will be required to pay a royalty on net sales of the product, if any.

Out-License Agreements

Eleison —In February 2011, the Company entered into an agreement with Eleison Pharmaceuticals whereby it granted Eleison an exclusive license for CISPLATIN Lipid Complex. The license gives Eleison the right to develop, manufacture and commercialize CISPLATIN Lipid Complex. Payments totaling $1.0 million were received in 2011 and were recorded as license fee revenue.

Premacure (now Shire plc) —In May 2012, the Company entered into an agreement with Premacure (now Shire plc) pursuant to which the Company granted to Premacure an exclusive, worldwide license to develop, manufacture and commercialize IGF-1, with its natural binding protein, IGFBP-3, for the prevention and treatment of complications of preterm birth in exchange for royalty payments on commercial sales of IGF-1 (the "Premacure License Agreement"). In March 2013, the Company amended the Premacure License Agreement to provide Premacure with the option, exercisable by Premacure any time prior to April 30, 2013, to pay the Company $11.5 million (the "Buyout Amount") and assume any of the Company's royalty obligations to other parties in exchange for a fully paid license. On April 29, 2013, Premacure exercised this option and paid the Company $11.5 million in exchange for a fully paid license. The Company recorded this payment as other revenue in the three months ended June 30, 2013. The Company is not entitled to any additional future royalties from Premacure, and Premacure has assumed the Company's royalty obligations to other parties under the Premacure License Agreement.

Collaboration Agreements

Cystic Fibrosis Foundation Therapeutics, Inc. —In 2004 and 2009, the Company entered into research funding agreements with Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT) whereby it received $1.7 million and $2.2 million for each respective agreement in research funding for the development of its ARIKAYCE product. If ARIKAYCE becomes an approved product for CF in the US, the Company will owe payments totaling up to $13.4 million to CFFT that would be payable over a three-year period after approval as a commercialized drug in the US. Furthermore, if certain global sales milestones are met within 5 years of the drug commercialization, the Company would owe an additional payment of $3.9 million. Since there is significant development risk associated with ARIKAYCE, the Company has not accrued these obligations.

Therapure Biopharma Inc. —In February 2014, the Company entered into a Contract Manufacturing Agreement with Therapure Biopharma Inc. ("Therapure") for the manufacture of the Company's product ARIKAYCE. Pursuant to the agreement, the Company and Therapure collaborated to construct a production area for the manufacture of ARIKAYCE in Therapure's existing manufacturing facility in Mississauga, Ontario, Canada. Therapure manufactures ARIKAYCE for the

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

10. License and Collaboration Agreements (Continued)

Company on a non-exclusive basis. The agreement has an initial term of five years from the first date on which Therapure delivers ARIKAYCE to Insmed after Insmed obtains permits related to the manufacture of ARIKAYCE, and will renew automatically for successive periods of two years each, unless terminated by either party by providing the required two years' prior written notice to the other party. Notwithstanding the foregoing, the parties have rights and obligations under the agreement prior to the commencement of the initial term. Under the agreement, the Company is obligated to pay certain minimum amounts for the batches of ARIKAYCE produced each calendar year. The agreement allows for termination by either party upon the occurrence of certain events, including (i) the material breach by the other party of any provision of the agreement or the quality agreement expected to be entered into between the parties, or (ii) the default or bankruptcy of the other party. In addition, the Company may terminate the agreement for any reason upon no fewer than one hundred eighty days' advance notice. Costs incurred under this agreement will be recorded as a component of research and development expense until such time as the Company receives regulatory approvals for ARIKAYCE.

PARI Pharma GmbH —In July 2014, the Company entered into a Commercialization Agreement with PARI for the manufacture and supply of eFlow nebulizer device as optimized for use with the Company's proprietary liposomal amikacin for inhalation. The agreement has an initial term of fifteen years from the first commercial sale of ARIKAYCE pursuant to the licensing agreement (the "Initial Term"). The term of the agreement may be extended by the Company for an additional five years by providing written notice to PARI at the least one year prior to the expiration of the Initial Term. Notwithstanding the foregoing, the parties have certain rights and obligations under the agreement prior to the commencement of the Initial Term. The agreement allows for termination by either party upon the occurrence of certain events, including (i) the material breach by the other party of any provision of the agreement, (ii) the default or bankruptcy of the other party, or (iii) in limited circumstances, upon termination by the Company of the License Agreement between the parties.

SynteractHCR, Inc. —In December 2014, the Company, entered into Work Order 1, pursuant to a Master Agreement for services with SynteractHCR, Inc., ("Synteract") dated as of August 27, 2014, as amended on December 23, 2014, pursuant to which the Company retained Synteract to perform implementation and management services in connection with certain clinical trials pursuant to a specific protocol of pharmaceutical products under development by or under the control of the Company. Synteract is providing comprehensive services for the 212 study. In April 2015, the Company entered into a work order with Synteract to perform implementation and management services for protocol INS-312, a study in which all non-converters from the 212 study will be eligible to enter a separate open-label study.

Ajinomoto Althea, Inc. —In September 2015, the Company entered into a Commercial Fill/Finish Services Agreement (the "Fill/Finish Agreement") with Ajinomoto Althea, Inc., a Delaware corporation ("Althea"), for Althea to produce, on a non-exclusive basis, ARIKAYCE in finished dosage form. Under the Fill/Finish Agreement, the Company is obligated to pay a minimum of $2.7 million for the batches of ARIKAYCE produced each calendar year during the term of the Fill/Finish Agreement. The Fill/Finish Agreement is effective as of January 1, 2015, has an initial term that ends on December 31, 2017 and may be extended for additional two year periods upon mutual written agreement of the Company and Althea at least one year prior to the expiration of its then-current term.

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

11. Commitments and Contingencies

Commitments

The Company has an operating lease for office and laboratory space located in Bridgewater, NJ for which the initial lease term expires in November 2019. Future minimum rental payments under this lease are $3.8 million. The Company also leases office space in Richmond, VA, where the Company's corporate headquarters were previously located, through October 2016. Future minimum rental payments under this lease total approximately $0.4 million. During 2011, the Company recorded a net present value charge of $1.2 million in general and administrative expenses associated with vacating the Richmond facility. In December 2014, the Company entered into an agreement to sublet this space for the remainder of the lease term.

Rent expense charged to operations, net of rental income recorded, was $0.8 million, $1.3 million, and $1.0 million for the years ended December 31, 2015, 2014 and 2013, respectively. Rent expense is recorded on a straight-line basis over the term of the applicable leases. Future minimum rental cash payments required under the Company's operating leases as of December 31, 2015 are as follows (in thousands):

Year Ending in December 31:	
2016	$ 1,271
2017	996
2018	1,025
2019	964
2020	-
	$ 4,256

Legal Proceedings

From time to time, the Company is a party to various other lawsuits, claims and other legal proceedings that arise in the ordinary course of business. While the outcomes of these matters are uncertain, management does not expect that the ultimate costs to resolve these matters will have a material adverse effect on the Company's consolidated financial position, results of operations or cash flows.

INSMED INCORPORATED

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

12. Quarterly Financial Data (Unaudited)

The following table summarizes unaudited quarterly financial data for the years ended December 31, 2015 and 2014 (in thousands, except per share data).

	2015				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Revenues	$ -	$ -	$ -	$ -	$ -
Operating loss	$ (26,706)	$ (27,952)	$ (30,245)	$ (32,590)	$ (117,493)
Net loss	$ (27,369)	$ (28,607)	$ (30,962)	$ (31,245)	$ (118,183)
Basic and diluted net loss per share	$ (0.55)	$ (0.47)	$ (0.50)	$ (0.51)	$ (2.02)

	2014				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Revenues	$ -	$ -	$ -	$ -	$ -
Operating loss	$ (18,079)	$ (22,816)	$ (23,404)	$ (23,066)	$ (87,365)
Net loss	$ (14,298)	$ (23,224)	$ (23,990)	$ (17,647)	$ (79,159)
Basic and diluted net loss per share	$ (0.36)	$ (0.59)	$ (0.54)	$ (0.36)	$ (1.84)

Basic and diluted net loss per share amounts included in the above table were computed independently for each of the quarters presented. Accordingly, the sum of the quarterly basic and diluted net loss per share amounts may not agree to the total for the year.

13. Retirement Plan

The Company has a 401(k) defined contribution plan for the benefit for all US employees and permits voluntary contributions by employees subject to IRS-imposed limitations. Beginning in April 2015, the Company matches 100% of eligible employee contributions on the first 3% of employee salary (up to the IRS maximum). Employer contributions for the year ended December 31, 2015 were $0.4 million. There were no employer contributions in 2014 and 2013.

EXHIBIT INDEX

2.1	Agreement and Plan of Merger, dated December 1, 2010, among Insmed Incorporated, River Acquisition Co., Transave, LLC Transave, Inc. and TVM V Life Science Ventures GmbH & Co. KG (incorporated by reference from Exhibit 2.1 to Insmed Incorporated's Current Report on Form 8-K filed on December 2, 2010 (SEC file no. 000-30739)).
3.1	Articles of Incorporation of Insmed Incorporated, as amended through June 14, 2012 (incorporated by reference from Exhibit 3.1 to Insmed Incorporated's Annual Report on Form 10-K filed on March 18, 2013).
3.2	Amended and Restated Bylaws of Insmed Incorporated (incorporated by reference from Exhibit 3.1 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 6, 2015).
4.1	Specimen stock certificate representing common stock, $0.01 par value per share, of the Registrant (incorporated by reference from Exhibit 4.2 to Insmed Incorporated's Registration Statement on Form S-4/A (Registration No. 333-30098) filed on March 24, 2000).
10.1**	Insmed Incorporated Amended and Restated 2000 Stock Incentive Plan (incorporated by reference from Exhibit 10.3 to Insmed Incorporated's Form 10-Q filed on May 7, 2013).
10.2**	Insmed Incorporated 2013 Incentive Plan (incorporated by reference from Exhibit 99.1 to Insmed Incorporated's Registration Statement on Form S-8 filed on May 24, 2013).
10.3**	Insmed Incorporated 2015 Incentive Plan (incorporated by reference from Exhibit 99.1 to Insmed Incorporated's Registration Statement on Form S-8 filed on May 28, 2015).
10.4**	Form of Award Agreement for Restricted Stock Units issued to employees pursuant to the Insmed Incorporated 2013 Incentive Plan (incorporated by reference from Exhibit 10.3 to Insmed Incorporated's Form 10-K filed on March 6, 2014).
10.5**	Form of Award Agreement for Restricted Stock Units issued to directors pursuant to the Insmed Incorporated 2013 Incentive Plan (incorporated by reference from Exhibit 10.4 to Insmed Incorporated's Form 10-K filed on March 6, 2014).
10.6**	Form of Award Agreement for an Incentive Stock Option pursuant to the Insmed Incorporated 2013 Incentive Plan (incorporated by reference from Exhibit 10.5 to Insmed Incorporated's Form 10-K filed on March 6, 2014).
10.7**	Form of Award Agreement for a Non-Qualified Stock Option pursuant to the Insmed Incorporated 2013 Incentive Plan (incorporated by reference from Exhibit 10.6 to Insmed Incorporated's Form 10-K filed on March 6, 2014).
10.8**	Employment Agreement, dated December 2, 2010, between Insmed Incorporated and Dr. Renu Gupta (incorporated by reference from Exhibit 10.4 to Insmed Incorporated's Current Report on Form 8-K filed on February 1, 2011).

10.9**	Transition and Separation Agreement, dated March 26, 2014 and effective as of April 16, 2014, between Insmed Incorporated and Renu Gupta, M.D. (incorporated by reference from Exhibit 10.3 to Insmed Incorporated's Form 10-Q filed on May 8, 2014).
10.10**	Employment Agreement, effective as of September 10, 2012, between Insmed Incorporated and William Lewis (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on September 11, 2012).
10.11**	Employment Agreement, effective as of November 7, 2012, between Insmed Incorporated and Andrew Drechsler (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on November 7, 2012).
10.12	Loan and Security Agreement, dated as of June 29, 2012, by and between Insmed Incorporated and its domestic subsidiaries and Hercules Technology Growth Capital, Inc. (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on July 2, 2012).
10.12.1	Amendment No. 1 to Loan and Security Agreement, dated as of July 24, 2012, by and between Insmed Incorporated and its domestic subsidiaries and Hercules Technology Growth Capital, Inc. (filed herewith).
10.12.2	Amendment No. 2 to Loan and Security Agreement, dated as of November 25, 2013, by and between Insmed Incorporated and its domestic subsidiaries and Hercules Technology Growth Capital, Inc. (filed herewith).
10.12.3	Amendment No. 3 to Loan and Security, dated as of December 15, 2014, by and among Insmed Incorporated and its domestic subsidiaries and Hercules Technology Growth Capital, Inc., Hercules Capital Funding Trust 2012-1 and Hercules Capital Funding Trust 2014-1 (incorporated by reference from Exhibit 10.27 to Insmed Incorporated's Annual Report on Form 10-K filed February 27, 2015).
10.12.4	Amendment No. 4 to Loan and Security Agreement, dated as of June 9, 2015, by and among Insmed Incorporated and its domestic subsidiaries and Hercules Technology Growth Capital, Inc., Hercules Capital Funding Trust 2012-1 and Hercules Capital Funding Trust 2014-1 (filed herewith).
10.12.5	Amendment No. 5 to Loan and Security Agreement, dated as of December 22, 2015, by and among Insmed Incorporated and its domestic subsidiaries and Hercules Technology Growth Capital, Inc., Hercules Capital Funding Trust 2012-1 and Hercules Capital Funding Trust 2014-1 (filed herewith).
10.13+	Settlement, license and development agreement, dated March 5, 2007, between Insmed Incorporated, Insmed Therapeutic Proteins, Inc., Celtrix Pharmaceuticals, Tercica Inc., and Genentech, Inc. (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Quarterly Report on 10-Q filed on May 10, 2007 (SEC file no. 000-30739)).
10.14+	License agreement, dated April 25, 2008, between Transave, Inc. and PARI Pharma GmbH, and Amendments No. 1-4 thereto (incorporated by reference from Exhibit 10.22 to Insmed Incorporated's Annual Report on Form 10-K filed on March 18, 2013).

10.14.1*	Amendment No. 5 to License Agreement between Transave, Inc. and PARI Pharma GmbH, effective as of October 5, 2015 (filed herewith).
10.14.2*	Amendment No. 6 to License Agreement between Transave, Inc. and PARI Pharma GmbH, effective as of October 9, 2015 (filed herewith).
10.15**	Employment Agreement, effective as of July 29, 2013, between Insmed Incorporated and Christine Pellizzari (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Form 10-Q filed on November 5, 2013).
10.16**	Insmed Incorporated Senior Executive Bonus Plan (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Form 10-Q filed on November 5, 2013).
10.17	Lease, dated December 31, 2013, between Denver Road, LLC and Insmed Incorporated (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on January 3, 2014).
10.17.1	First Amendment to Lease, dated April 29, 2014, between Denver Road, LLC and Insmed Incorporated (filed herewith).
10.17.2	Second Amendment to Lease, dated November 20, 2015, between Denver Road, LLC and Insmed Incorporated (filed herewith).
10.18	Form of Indemnification Agreement entered into with each of the Company's directors and officers (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on January 16, 2014).
10.19+	Contract Manufacturing Agreement, dated February 7, 2014, between Insmed Incorporated and Therapure Biopharma Inc. (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Form 10-Q filed on May 8, 2014).
10.20+	Amending Agreement, dated March 13, 2014, between Insmed Incorporated and Therapure Biopharma Inc. (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Form 10-Q filed on May 8, 2014).
10.21+	Commercialization Agreement dated July 8, 2014 between Insmed Incorporated and PARI Pharma GmbH (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Form 10-Q filed on November 6, 2014).
10.22	Stock Purchase Agreement, dated as of December 15, 2014, by and between Insmed Incorporated and Hercules Technology Growth Capital, Inc. (incorporated by reference from Exhibit 10.28 to Insmed Incorporated's Form 10-K filed on February 27, 2015).
10.23+	Master Agreement for Services, dated as of August 27, 2014, by and between Insmed Incorporated and SynteractHCR, Inc. (incorporated by reference from Exhibit 10.29 to Insmed Incorporated's Form 10-K filed on February 27, 2015).
10.24+	Work Order 1, dated as of December 30, 2014, by and between Insmed Incorporated and SynteractHCR, Inc. (incorporated by reference from Exhibit 10.30 to Insmed Incorporated's Form 10-K filed on February 27, 2015).

10.25**	Employment Agreement, effective as of February 18, 2014, between Insmed Incorporated and Peggy Berry (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Form 10-Q filed on May 7, 2015).
10.26**	Employment Agreement, effective as of January 2, 2013, between Insmed Incorporated and S. Nicole Schaeffer (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Form 10-Q filed on May 7, 2015).
10.27+	Commercial Fill/Finish Services Agreement between Insmed Incorporated and Ajinomoto Althea, Inc., dated as of September 15, 2015 (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Form 10-Q filed November 6, 2015).
21.1	Subsidiaries of Insmed Incorporated (filed herewith).
23.1	Consent of Ernst & Young LLP (filed herewith).
31.1	Certification of William H. Lewis, Chief Executive Officer of Insmed Incorporated, pursuant to Rules 13a- 14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes Oxley Act of 2003 (filed herewith).
31.2	Certification of William H. Lewis, Chief Executive Officer of Insmed Incorporated, pursuant to 18 USC Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2003 (filed herewith).
32.1	Certification of Andrew T. Drechsler, Chief Financial Officer (Principal Financial and Accounting Officer) of Insmed Incorporated, pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes Oxley Act of 2003 (filed herewith).
32.2	Certification of Andrew T. Drechsler, Chief Financial Officer (Principal Financial and Accounting Officer) of Insmed Incorporated, pursuant to 18 USC Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2003 (filed herewith).
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

+ The Securities and Exchange Commission has granted confidential treatment with respect to certain information in these exhibits. The confidential portions of these exhibits have been omitted and filed separately with the Securities and Exchange Commission.

* Confidential treatment has been requested for certain portions of this exhibit. The confidential portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission.

** Management contract or compensatory plan or arrangement of the Company required to be filed as an exhibit.

Exhibit 10.12.1

Execution Version

AMENDMENT NO. 1
TO
LOAN AND SECURITY AGREEMENT

THIS AMENDMENT NO. 1 TO LOAN AND SECURITY AGREEMENT (this " **Amendment** ") is entered into this 24th day of July, 2012 by and between **INSMED INCORPORATED** , a Virginia corporation (" **Parent** "), **INSMED PHARMACEUTICALS, INC.,** a Virginia corporation (" **Insmed Pharma** "), **CELTRIX PHARMACEUTICALS, INC.** a Delaware corporation (" **Celtrix** "), **TRANSAVE, LLC** , a Delaware limited liability company (" **Transave** ", together with Parent, Insmed Pharma, and Celtrix are hereinafter collectively referred to as the " **Borrowers** ", and each individually as a " **Borrower** "), and **HERCULES TECHNOLOGY GROWTH CAPITAL, INC.,** a Maryland corporation (the " **Lender** "). Capitalized terms used herein without definition shall have the same meanings given them in the Loan Agreement (as defined below).

RECITALS

A . Each Borrower and the Lender have entered into that certain Loan and Security Agreement dated as of June 29, 2012 (as amended, restated, supplemented or otherwise modified from time to time, the " **Loan Agreement** "), pursuant to which the Lender has agreed to extend and make available to the Borrowers certain extensions of credit.

B. Each Borrower and the Lender have agreed to amend the Loan Agreement upon the terms and conditions more fully set forth herein.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing Recitals and intending to be legally bound, the parties hereto agree as follows:

1 . **AMENDMENTS.**

1.1 Section 7.13 (Deposit Accounts). Section 7.13 of the Loan Agreement is hereby, retroactively to July 11, 2012, amended and restated in its entirety as follows:

> "7.13 Deposit Accounts. No Borrower nor any Subsidiary shall maintain any Deposit Accounts, or accounts holding Investment Property, except with respect to (a) which the Lender has an Account Control Agreement and (b) Wells Fargo Bank, National Association, account no. 070491230905172 (the " **Wells Fargo CD Account** "); provided, that (i) funds in the Wells Fargo CD Account shall not exceed $2,111,248 plus regularly accrued interest and (ii) all amounts in the Wells Fargo CD Account shall be transferred to an account with respect to which the Lender has an Account Control Agreement promptly upon the existing maturity date of the certificate of deposit on July 26, 2013."

2. BORROWERS' REPRESENTATIONS AND WARRANTIES . Each Borrower represents and warrants that:

(a) immediately upon giving effect to this Amendment (i) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct as of such date), and (ii) no Event of Default has occurred and is continuing;

(b) such Borrower has the corporate power and authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

(c) the certificate or articles of incorporation, bylaws and other organizational documents of such Borrower delivered to the Lender on the Closing Date remain true, accurate and complete and have not been amended, restated, supplemented or otherwise modified and continue to be in full force and effect;

(d) the execution and delivery by such Borrower of this Amendment and the performance by such Borrower of its obligations under the Loan Agreement, as amended by this Amendment, have been duly authorized by all necessary corporate action or limited liability company, as applicable, on the part of such Borrower;

(e) this Amendment has been duly executed and delivered by such Borrower and is the binding obligation of such Borrower, enforceable against it in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights generally; and

(f) as of the date hereof, such Borrower has no defenses against the obligations to pay any amounts under the Obligations.

Each Borrower understands and acknowledges that the Lender is entering into this Amendment in reliance upon, and in partial consideration for, the above representations and warranties, and agrees that such reliance is reasonable and appropriate.

3. LIMITATION. The amendments set forth in this Amendment shall be limited precisely as written and shall not be deemed (a) to be a waiver or modification of any other term or condition of the Loan Agreement or of any other instrument or agreement referred to therein or to prejudice any right or remedy which the Lender may now have or may have in the future under or in connection with the Loan Agreement or any instrument or agreement referred to therein; or (b) to be a consent to any future amendment or modification or waiver to any instrument or agreement the execution and delivery of which is consented to hereby, or to any waiver of any of the provisions thereof. Except as expressly amended hereby, the Loan Agreement shall continue in full force and effect.

4. EFFECTIVENESS. This Amendment shall become effective upon the satisfaction of all of the following conditions precedent in form and substance satisfactory to the Lender (the " **Effective Date** "):

4.1 **Amendment.** The Lender shall have received duly executed counterparts of this Amendment signed by the parties hereto.

5. **EXPENSES.** Each Borrower agrees to pay the Lender's costs and expenses (including the reasonable fees and expenses of the Lender's counsel, advisors and consultants) accrued and incurred in connection with the transactions contemplated by this Amendment, and all other Lender expenses (including the reasonable fees and expenses of the Lender's counsel, advisors and consultants) payable in accordance with Section 11.11 of the Loan Agreement.

6. **COUNTERPARTS.** This Amendment may be signed originally or by facsimile or other means of electronic transmission in any number of counterparts, and by different parties hereto in separate counterparts, with the same effect as if the signatures to each such counterpart were upon a single instrument. All counterparts shall be deemed an original of this Amendment.

7. **INTEGRATION.** This Amendment and any documents executed in connection herewith or pursuant hereto contain the entire agreement between the parties with respect to the subject matter hereof and supersede all prior agreements, understandings, offers and negotiations, oral or written, with respect thereto and no extrinsic evidence whatsoever may be introduced in any judicial or arbitration proceeding, if any, involving this Amendment; except that any financing statements or other agreements or instruments filed by the Lender with respect to the Borrowers shall remain in full force and effect.

8. **GOVERNING LAW; VENUE.** THIS AMENDMENT SHALL BE GOVERNED BY AND SHALL BE CONSTRUED AND ENFORCED IN ACCORDANCE WITH THE LAWS OF THE STATE OF CALIFORNIA. Each Borrower and the Lender each submit to the exclusive jurisdiction of the State and Federal courts in Santa Clara County, California.

[Remainder of page intentionally left blank; signature page follows]

IN WITNESS WHEREOF, the parties have duly authorized and caused this Amendment to be executed as of the date first written above.

BORROWERS:

INSMED INCORPORATED

By: /s/ Kevin P. Tully
Name: Kevin P. Tully
Title: Chief Financial Officer

INSMED PHARMACEUTICALS, INC.

By: /s/ Kevin P. Tully
Name: Kevin P. Tully
Title: Chief Financial Officer

TRANSAVE, LLC

By: /s/ Kevin P. Tully
Name: Kevin P. Tully
Title: Chief Financial Officer

CELTRIX PHARMACEUTICALS, INC.

By: /s/ Kevin P. Tully
Name: Kevin P. Tully
Title: Chief Financial Officer

LENDER:

HERCULES TECHNOLOGY GROWTH CAPITAL, INC.,

By: /s/ K. Nicholas Martitsch
Name: K. Nicholas Martitsch
Its: Associate General Counsel

Exhibit 10.12.2

AMENDMENT NO. 2
TO
LOAN AND SECURITY AGREEMENT

THIS AMENDMENT NO. 2 TO LOAN AND SECURITY AGREEMENT (this " ***Amendment*** ") is dated as of November 25, 2013 and is entered into by and among INSMED INCORPORATED, a Virginia corporation (" ***Parent*** "), INSMED PHARMACEUTICALS, INC., a Virginia corporation (" ***Insmed Pharma*** "), CELTRIX PHARMACEUTICALS, INC., a Delaware corporation (" ***Celtrix*** "), TRANSAVE, LLC, a Delaware limited liability company (" ***Transave*** ", together with Parent, Insmed Pharma, and Celtrix are hereinafter collectively referred to as the " ***Borrowers*** " and each individually as a " ***Borrower*** ''), and HERCULES TECHNOLOGY GROWTH CAPITAL, INC., a Maryland corporation (" ***Lender*** "). Capitalized terms used herein without definition shall have the same meanings given them in the Loan Agreement (as defined below).

RECITALS

A. Borrowers and Lender have entered into that certain Loan and Security Agreement dated as of June 29, 2012 (as may be amended, restated, supplemented or otherwise modified from time to time, the " ***Loan Agreement*** ''), pursuant to which Lender has extended and make available to Borrowers certain extensions of credit.

B. Borrowers and Lender have agreed to amend the Loan Agreement upon the terms and conditions more fully set forth herein.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing Recitals and intending to be legally bound, the parties hereto agree as follows:

1. AMENDMENTS.

1.1 The definition of "Amortization Date" in Section 1.1 is amended and restated with the following:

"Amortization Date" means July 1, 2014; provided that if Borrowers (i) achieve positive data from their TARGET-112 Phase II NTM Trial and (ii) pays Lender an additional $100,000 fee on or prior to July 1, 2014, then the Amortization Date shall be extended to January 1, 2015.

1.2 The reference to "$200,000" in clause (vii) of the definition of "Permitted Indebtedness" in Section 1.1 is hereby amended and restated with "$250,000".

1.3 The second sentence in Section 2.2(d) is amended and restated with the following:

The Borrowers shall repay the aggregate Term Loan principal balance that is outstanding on the Amortization Date in equal monthly installments of principal and interest (based upon a 30 month amortization schedule) commencing on the applicable Amortization Date and continuing on the first business day of each month thereafter with any yet to accrue amortization payments (balloon) due on the Term Loan Maturity Date.

2. BORROWERS' REPRESENTATIONS AND WARRANTIES. Each Borrower represents and warrants that:

(a) immediately upon giving effect to this Amendment (i) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct in all material respects as of such earlier date), and (ii) no Event of Default has occurred and is continuing;

(b) such Borrower has the corporate power and authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

(c) the certificate of incorporation, bylaws and other organizational documents of such Borrower delivered to Lender on the Closing Date remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

(d) the execution and delivery by such Borrower of this Amendment and the performance by such Borrower of its obligations under the Loan Agreement, as amended by this Amendment, have been duly authorized by all necessary corporate action on the part of such Borrower;

(e) this Amendment has been duly executed and delivered by such Borrower and is the binding obligation of such Borrower, enforceable against it in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights; and

(f) as of the date hereof, such Borrower has no defenses against the obligations to pay any amounts under the Obligations.

Each Borrower understands and acknowledges that Lender is entering into this Amendment in reliance upon, and in partial consideration for, the above representations and warranties, and agrees that such reliance is reasonable and appropriate.

3. LIMITATION. The amendments set forth in this Amendment shall be limited precisely as written and shall not be deemed (a) to be a waiver or modification of any other term or condition of the Loan Agreement or of any other instrument or agreement referred to therein or to prejudice any right or remedy which Lender may now have or may have in the future under or in connection with the Loan Agreement or any instrument or agreement referred to therein; or (b) to be a consent to any future amendment or modification or waiver to any instrument or agreement the execution and delivery of which is consented to hereby, or to any waiver of any of the provisions thereof. Except as expressly amended hereby, the Loan Agreement shall continue in full force and effect.

4. EFFECTIVENESS. This Amendment shall become effective upon the satisfaction of all the following conditions precedent:

4.1 Fee. The Borrowers shall pay Lender a non-renewable facility fee equal to $100,000.

4.2 **Amendment.** The Lender shall have duly executed counterparts of this Amendment signed by the parties hereto.

4.3 **Insurance Certificate.** The Lender shall have received insurance certificates reasonably satisfactory to Lender adding [DESCRIBE NEW ADDRESS] to such policies.

5. **COUNTERPARTS.** This Amendment may be signed in any number of counterparts, and by different parties hereto in separate counterparts, with the same effect as if the signatures to each such counterpart were upon a single instrument. All counterparts shall be deemed an original of this Amendment.

6. **INCORPORATION BY REFERENCE.** The provisions of Section 11 of the Agreement shall be deemed incorporated herein by reference, *mutatis mutandis.*

[signature page follows]

IN WITNESS WHEREOF, the parties have duly authorized and caused this Amendment to be executed as of the date first written above.

BORROWERS :

INSMED INCORPORATED

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: Chief Financial Officer

INSMED PHARMACEUTICALS, INC.

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: Chief Financial Officer

TRANSAVE, LLC

BY: INSMED INCORPORATED, ITS MANAGING MEMBER

By: /s/ Christine Pellizzari
Name: Christine Pellizzari
Title: General Counsel & Corporate Secretary

CELTRIX PHARMACEUTICALS, INC.

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: Chief Financial Officer

LENDER :

HERCULES TECHNOLOGY GROWTH CAPITAL, INC.

By: /s/ Ben Bang
Name: Ben Bang
Its: Senior Counsel

Exhibit 10.12.4

CONSENT AND AMENDMENT NO. 4
TO LOAN AND SECURITY AGREEMENT

This **CONSENT AND AMENDMENT NO. 4 TO LOAN AND SECURITY AGREEMENT** (this " ***Amendment*** ") is dated as of June 9, 2015 and is entered into by and among (a) **INSMED INCORPORATED** , a Virginia corporation ("Parent"), **INSMED PHARMACEUTICALS, INC.** , a Virginia corporation (" ***Insmed Pharma*** "), **CELTRIX PHARMACEUTICALS, INC.** , a Delaware corporation (" ***Celtrix*** "), **TRANSAVE, LLC** , a Delaware limited liability company (" ***Transave*** ", together with Parent, Insmed Pharma, and Celtrix are hereinafter collectively referred to as the " ***Borrowers*** " and each individually as a " ***Borrower*** "), and (b) **HERCULES TECHNOLOGY GROWTH CAPITAL, INC.** , a Maryland corporation (" ***Hercules Growth*** "), **HERCULES CAPITAL FUNDING TRUST 2012-1** , a statutory trust created and existing under the laws of the State of Delaware (" ***Hercules 2012*** "), and **HERCULES CAPITAL FUNDING TRUST 2014-1** , a statutory trust created and existing under the laws of the State of Delaware (" ***Hercules 2014*** ", together with Hercules Growth and Hercules 2012 collectively referred to as the " ***Lender*** "). Capitalized terms used herein without definition shall have the same meanings given them in the Loan Agreement (as defined below).

RECITALS

A. Borrowers and Lender have entered into that certain Loan and Security Agreement dated as of June 29, 2012, as amended by that certain Amendment No. 1 to Loan and Security Agreement dated as of July 24, 2012, as amended by that certain Amendment No. 2 to Loan and Security Agreement dated as of November 25, 2013, and as further amended by that certain Amendment No. 3 to Loan and Security Agreement dated as of December 15, 2014 (as may be further amended, restated, supplemented or otherwise modified from time to time, the " ***Loan Agreement*** "), pursuant to which Lender has extended and make available to Borrowers certain extensions of credit.

B. Borrowers notified Lender that Parent (a) has created a wholly-owned Subsidiary, Insmed Holdings Limited, a company organized under the laws of Ireland (" ***Holdings*** "), (b) has permitted Holdings to create a wholly-owned Subsidiary, Insmed Ireland Limited, a company organized under the laws of Ireland (" ***Irish Subsidiary*** "), (c) has permitted Irish Subsidiary to create four (4) wholly-owned Subsidiaries: (i) Insmed Germany GmbH, a company organized under the laws of Germany, (ii) Insmed Netherlands BV, a company organized under the laws of the Netherlands, (iii) Insmed France SAS, a company organized under the laws of France, and (iv) Insmed Limited, a company organized under the laws of England and Wales, (d) intends to permit Irish Subsidiary to create a wholly-owned Subsidiary organized under the laws of Italy ((a)-(d), collectively, the " ***Subsidiary Formation*** "), and (e) has licensed the Intellectual Property set forth on Schedule 1 hereto to Irish Subsidiary (the "License") pursuant to the terms and conditions of (i) that certain Cost Sharing Agreement effective as of April 1, 2015 by and among Parent and Irish Subsidiary attached as Schedule 2 hereto, and (ii) that certain Platform Contribution Transaction Intangible Property License Agreement effective as of April 1, 2015 by and among Parent and Irish Subsidiary attached as Schedule 3 hereto. Borrowers have requested that Lender consent to and ratify the Subsidiary Formation and the License.

C. Lender has agreed to so consent to and ratify the Subsidiary Formation and the License, but only to the extent, in accordance with the terms, subject to the conditions and in reliance upon the representations and warranties set forth below.

D. Borrowers and Lender have agreed to amend the Loan Agreement upon the terms and conditions more fully set forth herein.

E. Lender has agreed to so amend certain provisions of the Loan Agreement, but only to the extent, in accordance with the terms, subject to the conditions and in reliance upon the representations and warranties set forth below.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing Recitals and intending to be legally bound, the parties hereto agree as follows:

1. AMENDMENT.

1.1 Section 1.1 (Definitions and Rules of Construction). Clause (xi) appearing in the definition of "Permitted Investments" set forth in Section 1.1 of the Loan Agreement shall be amended in its entirety and replaced with the following:

> (xi) Investments in Subsidiaries organized outside of the United States for current, ordinary, and necessary operating expenses, not to exceed Fifteen Million Dollars ($15,000,000.00) in the aggregate in any calendar year, provided that no Event of Default has occurred and is continuing or would exist after giving effect to such Investment;

2. CONSENT AND RATIFICATION . Subject to the terms of Section 5 below, Lender (a) consents to and ratifies the Subsidiary Formation and agrees that the Subsidiary Formation shall not, in and of itself, constitute an "Event of Default" under Section 7.10 of the Loan Agreement (relative to mergers and acquisitions), and (b) consents to and ratifies the License and agrees that the License shall be considered a Permitted Transfer and shall not, in and of itself, constitute an "Event of Default" under Section 7.9 of the Loan Agreement (relative to transfers).

3. BORROWERS' REPRESENTATIONS AND WARRANTIES . Each Borrower represents and warrants that:

(a) immediately upon giving effect to this Amendment (i) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct as of such date), and (ii) no Event of Default has occurred and is continuing;

(b) such Borrower has the corporate or limited liability company, as applicable, power and authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

(c) the certificate of incorporation, bylaws and other organizational documents of such Borrower delivered to Lender on the Closing Date remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

(d) the execution and delivery by such Borrower of this Amendment and the performance by such Borrower of its obligations under the Loan Agreement, as amended by this Amendment, have been duly authorized by all necessary corporate or limited liability company, as applicable, action on the part of such Borrower;

(e) this Amendment has been duly executed and delivered by such Borrower and is the binding obligation of such Borrower, enforceable against it in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights; and

(f) as of the date hereof, such Borrower has no defenses against the obligations to pay any amounts under the Secured Obligations.

Each Borrower understands and acknowledges that Lender· is entering into this Amendment in reliance upon, and in partial consideration for, the above representations and warranties, and agrees that such reliance is reasonable and appropriate.

4. LIMITATION . The terms set forth in this Amendment shall be limited precisely as written and shall not be deemed (a) to be a waiver or modification of any other term or condition of the Loan Agreement or of any other instrument or agreement referred to therein or to prejudice any right or remedy which Lender may now have or may have in the future under or in connection with the Loan Agreement or any instrument or agreement referred to therein; or (b) to be a consent to any future amendment or modification or waiver to any instrument or agreement the execution and delivery of which is consented to hereby, or to any waiver of any of the provisions thereof. Except as expressly amended hereby, the Loan Agreement shall continue in full force and effect.

5. EFFECTIVENESS . This Amendment shall become effective upon the satisfaction of all the following conditions precedent:

5.1 Borrowers shall not license any of Borrowers' property or assets in connection with the License other than assets set forth on Schedule 1 hereto.

5.2 The Subsidiary Formation and the License do not otherwise result in an Event of Default after giving effect to such Subsidiary Formation and License.

5.3 Borrowers shall have paid all of Lender's reasonable, documented costs and out-of-pocket expenses in connection with this Amendment.

5.4 Lender shall have received duly executed counterparts of this Amendment signed by the parties hereto.

6. **COUNTERPARTS** . This Amendment may be signed in any number of counterparts, and by different parties hereto in separate counterparts, with the same effect as if the signatures to each such counterpart were upon a single instrument. All counterparts shall be deemed an original of this Amendment.

7. **INCORPORATION BY REFERENCE** . The provisions of Section 11 of the Loan Agreement shall be deemed incorporated herein by reference, *mutatis mutandis* .

[signature page follows]

IN WITNESS WHEREOF , the parties have duly authorized and caused this Amendment to be executed as of the date first written above.

BORROWERS :

INSMED INCORPORATED

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: CFO

INSMED PHARMACEUTICALS, INC.

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: CFO

TRANSAVE, LLC

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: CFO

CELTRIX PHARMACEUTICALS, INC.

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: CFO

[Signature page to Consent and Amendment No. 4 to Loan and Security Agreement]

LENDER :

HERCULES CAPITAL FUNDING TRUST 2012-1

By: Hercules Technology Growth Capital, Inc., its servicer

By: /s/ Bob Bang
Name: Bob Bang
Title: Associate General Counsel

HERCULES CAPITAL FUNDING TRUST 2014-1

By: Hercules Technology Growth Capital, Inc., its servicer

By: /s/ Bob Bang
Name: Bob Bang
Title: Associate General Counsel

HERCULES TECHNOLOGY GROWTH CAPITAL, INC.

By: Hercules Technology Growth Capital, Inc., its servicer

By: /s/ Bob Bang
Name: Bob Bang
Title: Associate General Counsel

[Signature page to Consent and Amendment No. 4 to Loan and Security Agreement]

Schedule 1

Schedule 1

Detail of Products Related to the Intangible Property Rights

Insmed Incorporated ("Insmed") has granted a license with respect to the Intangible Property Rights, as defined in the Platform Contribution Transaction ("PCT") Intangible Property License Agreement, effective as of April l, 2015, by and between Insmed Ireland limited and Insmed (the "Agreement"),related to the patents and products associated with:

1. ARIKAYCE
2. INS-1009
3. Any other products or development currently owned by Insmed prior to the execution of the Agreement.

Schedule 2

COST SHARING AGREEMENT

INSMED INCORPORATED - INSMED IRELAND LIMITED

This COST SHARING AGREEMENT (the " **Agreement** ") is effective as of April 1, 2015 (the "Effective Date"). by and between Insmed Ireland Limited ("Insmed Ireland"), a limited liability company organized under the laws of Ireland, with registered office at 25-28 North Wall Quay, Dublin 1, Ireland, registered with the Registrar of Companies under number 550604 and Insmed Incorporated ("Insmed U.S."), a corporation organized under the laws of Virginia with principal place of business at 10 Finderne Avenue, Building 10, Bridgewater, New Jersey (collectively, the " **Parties** " and individually, " **Party** ").

RECITALS

WHEREAS , the Parties are engaged in the business of researching, developing, marketing and distributing pharmaceuticals products (collectively "Insmed Group Property");

WHEREAS , the Parties have concurrently entered into a Platform Contribution Transaction ("PCT") Intangible Property License Agreement, dated as of the date herewith, pursuant to which Insmed Ireland acquired an exclusive license to license Developed Intangible Property Rights within the Insmed Ireland Field of Use in exchange for consideration, pursuant to U.S. Treas. Reg. Sec. 1.482-7(h)(2)(i)(B);

WHEREAS , the Parties desire to pool their resources for the purpose of further developing and otherwise enhancing the value of the Insmed Group Property, and of utilizing the Developed Intangible Property Rights in their respective Field of Use; and

WHEREAS , the Parties intend that the arrangement contemplated by this Agreement is a cost sharing arrangement within the meaning of U.S. Treas. Reg. Sec. 1.482-7(b).

NOW, THEREFORE , in consideration of the mutual covenants and promises hereinafter set forth, and other good and valuable consideration, receipt of which is hereby acknowledged, the Parties hereto agree as follows:

ARTICLE 1
EFFECTIVENESS OF RECITALS/DEFINITIONS

The Recitals set forth above are an integral part of this Agreement and shall have the same contractual and legal significance as any other language in this Agreement. For purposes of this Agreement, the following definitions shall apply to the terms set forth below wherever they appear:

Section 1.1 " **Affiliate** " or " **Affiliates** " of a Party means any entity controlled by, controlling or under common control with such Party, where control" in any of the foregoing forms means ownership, either direct or indirect, of more than fitly percent (50%) of the equity interest entitled to vote for the election of directors or equivalent governing body. An entity shall be considered an Affiliate only so long as such entity continues to meet the foregoing definition.

Section 1.2 " **Aggregate Allocable Intangible Development Costs** " for any Fiscal Year, or part thereof, means the sum of the Intangible Development Costs of both Parties for such Fiscal Year, or part thereof, less Specific In tangible Development Costs, as calculated under Article 2.

Section 1.3 " **Annual CSA Report** " means the document prepared by the Parties as provided in Article 3.

Section 1.4 " **Cost Share** " and " **Cost Share Percentage** " for any Fiscal Year shall be the amounts respectively specified for those terms in Section 3.5.

Section 1.5 " **Developed Intangible Property Rights** " means any and all rights relating to the Developed Technology and the Developed Marketing Intangibles and arising from or developed as a result of the Intangible Development Activity on or after the Effective Date (by whatever name or term known or designated), including, without limitation:

(a) all inventions, know-how, technical data, trade secrets, functional or detailed design specifications, designs and enhancements, whether patentable or un-patentable, patented or un-patented;

(b) all trademarks, copyrights, service marks and trade name rights, internet domain names, social media designations, and other designations and similar rights;

(c) all franchises, licenses, or contracts;

(d) all rights associated with works of authorship throughout the world, including but not limited to copyrights, moral rights and software;

(e) all Patents (including provisionals, continuations, continuations-in-part, and divisionals thereof), reissues and re-examinations thereof, database rights, design rights and other industrial property rights that have the benefit of a filing date on or after the Effective Date;

(f) all patent applications (including continuations, continuations-in-part and divisionals thereof) now or hereafter in force, that have the benefit of a filing date on or after the Effective Date;

(g) all rights, including copyrights, source code, Confidential Information and trade secrets underlying the technology and any prints, packaging, labels, advertising or promotional material and any other materials of any kind using or used in conjunction with trademarks and know how underlying the developed marketing intangibles, whether created by the Parties their Affiliates or any Third Party engaged by the Patties or their Affiliates to create any thereof; and

(h) any additional applicable intangible property as defined under U.S. Treas. Reg. Sec. 1.482-4(b) (whether or not in documentary form and whether or not patentable, copyrightable, or otherwise protectable under applicable laws).

Section 1.6 " **Developed Marketing Intangibles** " means and includes any and all trademarks, trade names, service marks, copyrights, domain names, applications and registrations of any of the foregoing, packaging, marketing strategies, customer lists or relationships, and other marketing information used in the marketing and promotion of the Insmed Group Property, arising from or developed as a result of the Intangible Development Activity on or after the Effective Date.

Section 1.7 " **Developed Technology** " means and includes any and all technologies, products, inventions, updates, adaptations, know-how, technical data, source code, trade secrets, functional or detailed specifications, labels, designs and enhancements of any of the foregoing, whether patentable or un-patentable, registered or unregistered, underlying the Insmed Group Property, arising from or developed as a result of the Intangible Development Activity on or after the Effective Date.

Section 1.8 " **Field of Use** " of a Party means the Insmed Ireland Field of Use or the Insmed U.S. Field of Use. as the case may be.

Section 1.9 " **Fiscal Year** " means the period from January 1 to December 3 I of each year. " **Fiscal Quarter End** " means the quarters ending March 31, June 30, September 30, and December 3 I and "Fiscal Year End" means the year ending December 31.

Section 1.10 " **Gross Profit** " means revenue recognized from the sale or license of the Products minus costs of goods sold associated with those Products determined in accordance with U.S. Generally Accepted Accounting Principles ("GAAP").

Section 1.11 " **Insmed Ireland Field of Use** " means all jurisdictions throughout the world, except for the United States of America or as mutually agreed upon from time to time in writing by the Parties.

Section 1.12 " **Insmed Group Property** " means the comprehensive suite of Insmed products comprised of the pharmaceutical products and development and other intangible property used to develop or distribute Insmed Group Property.

Section 1.13 " **Insmed U.S. Field of Use** " means the United States of America, or as mutually agreed upon from time to time in writing by the Parties.

Section 1.14 " **Intangible Development Activity** " means the activities or either Party under this Agreement with respect to Insmed Group Property that give rise to Intangible Development Costs.

Section 1.15 " **Intangible Development Costs** " of a Party shall be the amounts specified for that term in Article 2.

Section 1.16 " **Products** " means any and all items sold incorporating the intangibles acquired or maintained under the PCT Intangible Property License Agreement and /or Developed Intangible Property Rights, and any other products specified by the Parties.

Section 1.17 " **Representative(s)** " means and includes all employees, managers, officers, directors, partners, consultants, independent contractors, licensees, successors. assigns and agents, of a Party.

Section 1.18 " **Specific Development** " means any Developed Technology or Developed Intangible Property Rights which, as between Insmed U.S. and Insmed Ireland, can be utilized solely by, or is of benefit solely to, either Insmed U.S. or Insmed Ireland, as the case may be.

Section 1.19 " **Specific Intangible Development Costs** " means Intangible Development Costs incurred during a Fiscal Year, or part thereof, by either Insmed U.S. or Insmed Ireland with respect to any particular Specific Development.

Section 1.20 " **Sub-licensee** " means any Affiliate of a Party or any Third Party to whom a Party sublicenses or transfers any portion of its rights under this Agreement to use the Developed Intangible Property Rights within such Party's Field of Use, and who agrees in writing to be bound by and to comply with all of the terms, conditions and obligations pertaining to "Sub-licensees" under this Agreement.

Section 1.21 " **Third Party** " means and includes any individual, corporation, trust, estate, partnership, joint venture, company, association, league, governmental bureau or agency or any other entity regardless of the type or nature, which is not a Party or an Affiliate.

ARTICLE 2
INTANGIBLE DEVELOPMENT COSTS

Section 2.1 Specific Intangible Development Costs . All Specific Intangible Development Costs shall be allocated in their entirety to the Party to whom the particular Specific Development pertains.

Section 2.2 Intangible Development Costs . Intangible Development Costs of a Party shall include the following:

(a) All costs incurred by such Party from activities directly or indirectly relating to the creation or improvement of Developed Intangible Property Rights on or after the Effective Date; and

(b) Stock-based compensation granted to employees whose salaries are included in the cost of the Developed Intangible Property Rights, on or after the Effective Date.

Section 2.3 Determination of Costs . The following principles shall apply in the determination of Intangible Development Costs:

(a) Intangible Development Costs shall be determined in accordance with expenses recognized under U.S. GAAP as applied by Insmed U.S. for financial reporting purposes; provided, however, that: (i) such costs shall not include acquisition costs for land or depreciable property, interest expense or foreign or domestic income taxes incurred; and (ii) such costs shall include a reasonable rental charge for the use of any land or depreciable tangible personal property used in connection with the Intangible Development Activity. For

administrative convenience, the Parties agree that, absent any evidence to the contrary, a reasonable rental charge shall be equal to depreciation or amortization expense recognized for any such item of property used in connection with the Intangible Development Activity. Intangible Development Costs shall include direct costs of the relevant activities and an allocable share of administrative or overhead costs. Where any indirect costs or direct costs benefit both Aggregate Allocable Intangible Development Costs and Specific Intangible Development Costs, an allocation shall be made using methods that are mutually agreed to be consistent, reasonable and in keeping with sound accounting practices.

(b) The stock-based compensation port ion of Intangible Development Costs shall be calculated in a manner consistent with U.S. Treas. Reg. Sec. 1.482-7(d)(3)(iii)(B).

(c) For the avoidance of doubt; the Parties shall use a consistent method of accounting to determine the Intangible Development Costs under this Section 2.3 and the Cost Share Percentages under Section 3.5 and must translate currencies on a consistent basis.

Section 2.4 Intangible Development Costs Budget . Before or during each Fiscal Year, the Parties shall agree on a budget of Intangible Development Costs expected to be incurred pursuant to the Intangible Development Activity during that Fiscal Year.

ARTICLE 3
INTANGIBLE DEVELOPMENT COST ALLOCATION

Section 3.1 Annual CSA Report . As soon as practical after the closing of the annual financial statements of each Party for each Fiscal Year End, the Parties shall each prepare necessary financial statements and forecasts, and shall jointly reconcile and consolidate such statements and forecasts into a report (the " **Annual CSA Report** "} containing the information required by this Article 3.

Section 3.2 Determination of Aggregate Allocable Intangible Development Costs . The Annual CSA Report shall indicate the types and amounts of Intangible Development Costs incurred by each Party from the first day of such Fiscal Year through such Fiscal Year End, comprising the Aggregate Allocable Intangible Development Costs. Such Aggregate Allocable Intangible Development Costs shall be determined annually and paid in accordance with Section 3.4, Section 4.1, Section 4.3, Section 4.4 and Section 4.6 as well as reconciled annually in accordance with Section 3.6, Section 3.7 and Section 4.2.

Section 3.3 Measure of Reasonably Anticipated Benefits . The Parties agree to share the Aggregate Allocable Intangible Development Costs under the terms specified in this Agreement. Aggregate Allocable Intangible Development Costs of the Intangible Development Activity shall be borne by each Party based upon the reasonably anticipated benefits (‘“RAB”) to be derived by each Party as a result of utilization of the Developed Intangible Property Rights. The Parties have determined that the most reliable basis for measuring RAB to be derived by them from Developed Intangible Property Rights is Gross Profit projected to be derived by them within their Field of Use for the then current Fiscal Year and all Fiscal Years over the remaining life of IP; however, if in subsequent years a different basis is determined to be more reliable, this basis ma y be used instead if mutually agreed to by the Parties in writing. The Parties believe that

each Party's respective ratio of Gross Profit for all Insmed Group Property is related to income generated or costs saved by the Parties. The Parties agree to periodically adjust how Aggregate Allocable Intangible Development Costs are shared to appropriately reflect any changes in economic conditions, their business operations and practices and the ongoing research and development efforts under this Agreement.

Section 3.4 Cost Share and Cost Share Percentage . A Party's "Cost Share Percentage" shall be the percentage equivalent of that Party's RAB to be derived from utilizing the Developed Intangibles over the sum of each Party's Reasonably Anticipated Benefits to be derived from utilizing the Developed Intangibles, as determined under Section 3.4 (Measure of Anticipated Benefits) of this Agreement. A Party's "Cost Share" tor a particular Fiscal Year shall be the Aggregate Allocable Intangible Development Costs for that Fiscal Year multiplied by that Party's Cost Share Percentage. The supporting documentation shall include a determination of each Party's Cost Share Percentage and Cost Share. The Annual CSA Report shall include a determination of each Party's Cost Share Percentage and Cost Share. For the avoidance of doubt, the Parties shall use a consistent method of accounting to determine the Intangible Development Costs under Section 2.3 and the Cost Share Percentages under this Section 3.4 and must translate currencies on a consistent basis.

Section 3.5 Calculations, Amendments and Compensating Adjustments . The Parties anticipate applying, amending and updating the calculations specified i n Section 3.2 and Section 3.4 as follows:

(a) As soon as practical after each Fiscal Year End, the Parties shall calculate the projected Gross Profit to be applied to the current Fiscal Year and the Aggregate Allocable Intangible Development Costs for the current Fiscal Year;

(b) As soon as practical after each Fiscal Quarter End, the Parties shall calculate the net Quarterly Payment Amount specified in Section 4.1 by (1) calculating each Party's Cost Share for such Fiscal Quarter End under Section 3.4, (2) adding each Party's Specific Intangible Development Costs for such Fiscal Quarter End under Section 2.1, and (3) subtracting the amount of Intangible Development Costs incurred by each Party during the Fiscal Quarter End.

(c) The Parties shall continue to perform the calculation steps outlined in Section 3.6(a) through this Section 3.6(c) for successive Fiscal Years.

Section 3.6 Reconciliation of Prior Year Cost Shares . The Annual CSA Report shall include a reconciliation of all prior year Cost Share computations that relied on forecasts of current Fiscal Year financial results. The prior year Cost Share Percentages shall be recomputed replacing the prior forecasts with the most recent actual data and forecasts available and for any revisions to the RAB. Potential adjustments shall be determined for all prior years, in accordance with the cumulative application of actual financial results specified in Section 3.5(b), for which either Party's Cost Share Percentage differs by more than twenty percent (20%) from the Cost Share Percentage recomputed under this Section 3.6, unless such difference is due to an extraordinary event beyond the control of the Parties that could not reasonably have been

anticipated. Adjustments for prior years may also be determined upon mutual agreement by the Parties.

ARTICLE 4
PAYMENTS

Section 4.1 Quarterly Payment Amount . The Parties shall pay the net amount to reconcile their quarterly Intangible Development Costs incurred with their quarterly relative Cost Share Percentage as applied to the Aggregate Allocable Intangible Development Costs. Such amounts are specified in Section 3.2 (Determination of Aggregate Allocable Intangible Development Costs) and Section 3.5 (Cost Share and Cost Share Percentage), respectively.

Section 4.2 Year-End Settlement Amount . The Parties shall pay the net amount to reconcile their annual Intangible Development Costs incurred with their annual relative Cost Share Percentage as applied to the Aggregate Allocable Intangible Development Costs. Such amounts are specified in Section 3.2 (Determination of Aggregate Allocable Intangible Development Costs) and Section 3.5 (Cost Share and Cost Share Percentage), respectively (the "Year-End Settlement Amount"). The Year-End Settlement Amount shall take into account amounts determined under Section 3.6 (Calculations, Amendments and Compensating Adjustments).

Section 4.3 Timing of Payments . Within sixty (60) days following the Fiscal Quarter End, commencing with the first quarter following the Effective Date of this Agreement, the Parties shall pay the amount due under Section 4.1 (Quarterly Payment Amount). Similarly, within sixty (60) days following the Fiscal Year end, commencing with the first Fiscal Year End following the Effective Date of this Agreement, the Parties shall pay the amount due under Section 4.2 (Year-End Settlement Amount). When applicable, interest based upon U.S. Treasury Regulations§ 1.482-2(a) shall be applied.

Section 4.4 Manner of Payment . All payments under this Article 4 shall be made in accordance with the policies and procedures of the Parties. Payment may be made by either Party under any reasonable method agreed upon by the Parties, including without limitation, in the form of a bank draft, wire transfer, note or, to the extent allowable under applicable law, a netting of amounts due from one Party to the other Party under this Agreement against existing accounts receivable by the first mentioned Party from the other Party. In the event payment is made by way of netting, such payment shall be effective as of the date of the netting on the books of the Parties.

Section 4.5 Records and Audits .

(a) Each Party shall each keep and maintain complete and accurate records of the transactions underlying the payments to be made hereunder for at least seven (7) years and, promptly upon request, shall allow the other Party or its designee to inspect, audit and make extracts or copies of such records for the purpose of ascertaining the correctness of such payments. If an y examination or audit discloses any overpayment or underpayment, the appropriate Party shall pay the deficiency plus interest thereon at the U.S. Applicable Federal Rate under U.S. Treas. Reg. Sec. 1.482-2(a), compounded annually from the date the deficiency

was due to the other Party, within a reasonable time after the conclusion of such examination or audit.

(b) Each Party shall comply with the documentation, accounting and reporting requirements, as prescribed under U.S. Treas. Reg. Sec. 1.482-7(k)(2)-(4), including but not limited to the following:

(i) each Party agrees to file a Settlement of Controlled Participant to Section 1.482-7 Cost Sharing Arrangement (" **Statement** ") with the Internal Revenue Service no later than ninety (90) days after the first occurrence of an Intangible Development Cost; and

(ii) each Party also agrees, during the term of this Agreement, to annually attach a copy of such Statement, or an updated version of such Statement, if required, to its U.S. income tax return, or if no such income tax return is required, to Schedule M of any Form 5471, Form 5472 or Form 8865 filed with respect to such Party.

Section 4.6 Currency . All payments contemplated hereby or made by either Party in connection herewith shall be made in U.S. Dollars or in a currency as mutually agreed to by the Parties. Any reported amount in currencies other than the U.S. Dollars shall be translated into U.S. Dollars at the prevailing bookkeeping rate used by the Parties during the period in which the amount is recognized under U.S. GAAP as applied for financial reporting purposes.

Section 4.7 Assumption of Development Risk . Each Party shall bear its Cost Share in accordance with the terms of this Agreement without regard to the success or failure of the Intangible Development Activity or the commercial viability of the Developed Intangible Property Rights.

Section 4.8 Platform Contribution Transactions . For all platform contributions under U.S. Treas. Reg. Sec. 1.482-7(c) occurring with respect to the Intangible Development Activity after the Effective Date, the Patties commit to engage in further platform contribution transactions ("PCTs") as follows:

(a) The Party that develops, maintains or acquires such resource, capability or right shall make such resource, capability or right available to the Intangible Development Activity as of the date it is developed, maintained or acquired;

(b) The other Party shall make arm's length payments to the first mentioned Party pursuant to U.S. Treas. Reg. Sec. 1.482-7(b)(l)(ii); and

(c) Unless otherwise specified by the Parties, the form of payment for all PCTs will be contingent payments pursuant to U.S. Treas. Reg. Sec. 1.482-7(h)(2)(i)(B).

To the extent a platform contribution arises from an asset acquisition, each Party shall be treated as if it acquired its share of the related resource, capability or right directly from the seller.

ARTICLE 5
OWNERSHIP OF AND LICENSES UNDER DEVELOPED INTANGIBLE PROPERTY RIGHTS

Section 5.1 Bare Legal Title . For administrative convenience only, bare legal title to the Developed Intangible Property Rights shall remain with the Party registered, to utilize fully anywhere in the world, subject to the rights of the Parties under this Agreement, including without limitation, under Section 5.2. For the avoidance of doubt, unless otherwise specified in this Agreement, the Parties hold the following rights: (i) the right to control the quality standard relative to the Developed Intangible Property Rights; (ii) the right to apply for and obtain registrations for the Developed Intangible Property Rights; (iii) the right to enforce the Developed Intangible Property Rights against Third Parties; (iv) the right to defend Third Party objections to or claims against the Developed Intangible Property Rights; and (v) the right to maintain and abandon the applications, registrations and other statutory rights in and to the Developed Intangible Property Rights. For purposes of interpretation of this Section 5.1 under the Lanham (Trademark) Act, all use of trademarks will inure to the benefit of the Parties. All legal rights associated with the Developed Intangible Property Rights related thereto will automatically vest in the Parties at the time that such Developed Intangible Property Rights are first created.

Section 5.2 Beneficial Ownership; All Substantial Rights . Insmed U.S. shall have beneficial ownership of the Developed Intangible Property Rights in the Insmed U.S. Field of Use and Insmed Ireland shall have beneficial ownership of the Developed Intangible Property Rights in the Insmed Ireland Field of Use.

Section 5.3 Reciprocal Rights . So that Insmed Ireland may utilize the Developed Intangible Property Rights in its business and fully enjoy its beneficial ownership thereof, and unless otherwise mutually agreed to by the Parties in writing, Insmed U.S. grants to Insmed Ireland an exclusive, perpetual, royalty-free right and license in, to and under the Developed Intangible Property Rights to make, have made, develop, have developed, use, sell, offer to sell, import, perform, display, reproduce and distribute (through one or more tiers of distribution) the Insmed Group Property in the Insmed Ireland Field of Use, to make improvements, modifications and/or enhancements to the Insmed Group Property and the Developed Intangible Property Rights in the Insmed Ireland Field of Use and to sublicense the Developed Intangible Property Rights in the Insmed Ireland Field of Use (including the right to sublicense through one or more tiers of sub-licensees).

So that Insmed U.S. may utilize the Developed Intangible Property Rights in its business and fully enjoy its beneficial ownership thereof, and unless otherwise mutually agreed to by the Parties in writing, Insmed Ireland grants to Insmed U.S. an exclusive, perpetual, royalty-free right and license in, to and under the Developed Intangible Property Rights to make, have made, develop, have developed, use, sell,, offer to sell, import, perform, display, reproduce and distribute (through one or more tiers of distribution) the Insmed Group Property in the Insmed U.S. Field of Use, to make improvements, modifications and /or enhancements to the Insmed Group Property and the Developed Intangible Property Rights in the Insmed U.S. Field of Use and to sublicense the Developed Intangible Property Rights in the Insmed U.S. Field of Use (including the right to sublicense through one or more tiers of sub-licensees).

Section 5.4 Disclosure for Purposes of the Intangible Development Activity . During the term of this Agreement, the Parties shall make available to each other all Developed Intangible Property Rights for the purpose of enabling each other to undertake and continue their respective participation in the Intangible Development Activity. Developed Intangible Property Rights may be furnished in documentary or consultative form at such time and in such manner as may be mutually convenient to the Parties.

Section 5.5 No Waiver or Release . Making available Developed Intangible Property Rights under Section 5.4 shall not constitute any release or waiver by a Party of its rights in the Developed Intangible Property Rights. To the extent required or appropriate, solely for the purpose of establishing bare legal title to the Developed Intangible Property Rights in accordance with Section 5.1, and subject to the licenses granted in Section 5.2 and elsewhere in this Agreement:

(a) The Parties and Sub-licensees hereby assign all their rights, title and interest in and to the Developed Intangible Property Rights, including without limitation: (i) all rights under the United States Copyright Act or any other country's copyright law, including without limitation, any rights provided in 1 7 U.S.C. §§ 106 and 106A, and (ii) any rights of attribution and integrity or any other "moral rights of authors" existing under statutory, common or any other law, and will execute and provide to the Parties documents and instruments of conveyance with respect to such Developed Intangible Property Rights as may be appropriate to perfect title thereto. The absence of such written documentation shall not limit the rights of the Parties in the Developed Intangible Property Rights hereunder.

(b) To the extent any of the rights, title and interest in and to the foregoing Developed Intangible Property Rights cannot be assigned by the Parties and/or Sub-licensees, each Party and/or Sub-licensees hereby grant to the other Party a non-exclusive, royalty-free, transferable, perpetual, unrestricted, worldwide license (with rights to sublicense through one or more tiers of sub licensees) under such non-assignable Developed Intangible Property Rights.

(c) To the extent any of such Developed Intangible Property Rights can be neither assigned nor licensed by the Parties and/or Sub-licensees, the Parties and/or Sub-licensees hereby waive and agree never to assert their rights in any such non-assignable and non-licensable Developed Intangible Property Rights against either Party, their Affiliates, licensees or successors or its and their respective customers.

The Parties shall have an agreement in place with all of its Sub-licensees to enable each Party to satisfy and fulfill its obligations under this Section 5.5.

Section 5.6 Power of Attorney . Solely for the purpose of satisfying its obligations under Section 5.5, each Party hereby authorizes the other Party to make, constitute and appoint any representative, in its sole discretion, as true and lawful attorney-in-fact, with power to endorse that Party on all applications, documents, papers and instruments necessary or desirable to implement some, all or any of the rights that the Parties have assigned or agreed to assign under Section 5.5. The Parties hereby ratify all that such attorney shall do or cause to be done by virtue hereof.

Section 5.7 Mutual Cooperation and Notice . Each Party will cooperate fully with the other Party in the defense of any lawsuit, action, legal proceeding, claim or demand relating to the Developed Intangible Property Rights.

Section 5.8 Utilization of Developed Intangible Property Rights .

(a) To the extent practicable, the Parties shall jointly enter into all contracts or agreements for the worldwide utilization of the Developed Intangible Property Rights. Such contracts or agreements shall provide that each Party derives the benefits of utilization of the Developed Intangible Property Rights within such Party's Field of Use only. To the extent payments under such a contract or agreement are to be received by only one of the Parties, such Party shall act as collection agent for the other Party and shall rem it to such other Party the portion of such payment allocable to utilization of the Developed Intangible Property Rights within such other Party's Field of Use.

(b) To the extent it is not practicable for the Parties to jointly enter into a contract or agreement for the worldwide utilization of the Developed Intangible Property Rights, any such contract or agreement entered into by only one of the Parties shall provide for the utilization of the Developed Intangible Property Rights in such Party's Field of Use only.

ARTICLE 6
SCOPE, FUNCTIONS AND RISKS

Section 6.1 Scope of the Intangible Development Activity . The scope of the Intangible Development Activity shall be any and all activities involving the development of Developed Intangible Property Rights.

Section 6.2 Functions of the Parties . The Parties anticipate that each Party will perform or subcontract the performance of Intangible Development Activities in its respective Field of Use i n order to develop the Developed Technology, Developed Marketing Intangibles and underlying Developed Intangible Property Rights. The Parties also anticipate that each Party will market, sell and distribute (or license the right to market, sell and distribute) the Insmed Group Property in its respective Field of Use and will perform such general and administrative activities as are necessary to utilize the Developed Intangible Property Rights in its respective Field of Use.

Section 6.3 Risks of the Parties . Subject to any terms in this Agreement and any other agreement between the Parties to the contrary, the Parties acknowledge that each Party incurs the risk of funding Intangible Development Costs without guarantee of success under Section 4.7, the risk of developing and maintaining its Insmed Group Property, the risk that its customers or licensees may not pay any accounts receivable due and such other genera l business risks as relate to the functions listed in Section 6.2.

ARTICLE 7
CONFIDENTIAL INFORMATION

Section 7.1 Definition of Confidential Information . The Patties acknowledge that, from time to time, one Party (the " **Discloser** ") may disclose to the other Party (the " **Recipient** ")

information: (a) which is marked with "confidential" or a similar legend; (b) which is described orally and designated as confidential; (c) which would, under the circumstances, be understood by a reasonable person to be confidential; or (d) which is defined as confidential elsewhere in this Agreement (" **Confidential Information** "). Notwithstanding the foregoing, any unmarked or oral information between employees or Representatives of the Parties discussing Confidential Information will be Confidential Information by default whether or not declared confidential and whether or not it is subsequently described in writing. Upon subsequent disclosure of previously disclosed Confidential Information to the Recipient by the Discloser, the information will remain Confidential Information even if not identified as Confidential Information at the subsequent disclosure.

Section 7.2 Confidentiality Obligations . The Recipient shall retain such Confidential Information in confidence, and shall not disclose it to any Third Party or use it for other than the purposes of this Agreement without the Discloser's prior written consent, unless disclosure is made to the Recipient's professional consultants who are bound to confidentiality under their professional law (e.g. lawyers, tax advisers and auditors) excluding Securities Exchange Commission ("SEC") filings and investor presentations. Each Party shall use at least the same procedures and degree of care with respect to such Confidential Information which it uses to protect its own confidential information of like importance, and in no event less than reasonable care. The Recipient will immediately give written notice to the Discloser of any unauthorized use or disclosure of the Discloser's Confidential Information, and the Recipient will assist the Disc loser in remedying such unauthorized use or disclosure.

Section 7.3 Compelled Disclosure . In the event that the Recipient or (to the knowledge of the Recipient) any of its Representatives is requested or required (by oral questions, interrogatories, requests for information or documents in legal proceedings, subpoenas, civil investigative demands or other similar processes) to disclose any of the Discloser's Confidential Information, the Recipient shall provide the Discloser with prompt written notice of any such request or requirement sufficiently timely to allow the Discloser adequate time to seek a protective order or other appropriate remedy and/or waive compliance with the provisions of this Agreement.

Section 7.4 Exceptions . Notwithstanding the foregoing, Confidential Information will not include information to the extent that such information:

(a) was generally available to the public at the time' of its disclosure to the Recipient hereunder;

(b) became generally available to the public after its disclosure other than through an act or omission of the Recipient (or one of its employees, agents or Representatives) in breach of this Agreement; or

(c) was subsequently lawfully and independently disclosed to the Recipient by a person other than the Discloser without an obligation of confidentiality.

In the event that the Recipient intends to disclose to a Third Party any of the Discloser's Confidential Information under the exceptions (a), (b) or (c) above, the Recipient must first

obtain the Discloser's written permission to do so, which approval will be at the Discloser's sole discretion.

Section 7.5 Third Party Contracts . Prior to the Recipient's disclosure of any of the Discloser's Confidential Information to any Third Party, the Recipient must require the Third Party to enter into a nondisclosure agreement (" **NDA** ") provided by the Discloser; the NDA will take precedence over the Third Party agreement.

Section 7.6 Third Party Confidential Information . To the extent that any information is: (a) received by a Party from a Third Party and (b) such Party is under an obligation to such Third Party to maintain the confidentiality of such information, such information shall be deemed to be Third Party Confidential Information and the other Party, to the extent that such Third Party Confidential Information is disclosed to it hereunder, shall maintain the confidentiality of such Third Party Confidential Information in accordance with such obligation of confidentiality as if it had entered into such obligation with such Third Party.

Section 7.7 Ownership of Confidential Information . The Recipient agrees that all Confidential Information received, including, without limitation, files, lists, records, documents, drawings, models, source code, apparatus, sketches and specifications, which incorporate or refer to or embody all or a portion of the Confidential Information, is and will remain the property of the Discloser and that such Confidential Information shall not be copied or reproduced without the express permission of the Disc loser, except for such copies as may be reasonably necessary in order to accomplish the purpose of this Agreement. Upon written request of the Discloser, the Recipient shall immediately discontinue all use of all Confidential Information of the Discloser, other than such items of Confidential Information developed pursuant to this Agreement as may specifically relate to improvements/refinements to the Developed Intangible Property Rights, and shall, at the Discloser's option, either destroy or return to the Discloser all hard copies in its possession of such Confidential Information and any derivatives thereof (including all hard copies of any translation, modification, compilation, abridgement or other form in which the Confidential Information has been recast, transformed or adapted) and to delete all on-line electronic copies thereof; provided, however, that the Recipient may retain one (1) archival copy of the Confidential Information, which shall be used only in case of a dispute concerning this Agreement. Notwithstanding the foregoing, neither Party shall be required to destroy or alter any computer-based back-up files generated in the normal course of its business, provided that such files are maintained confidential in accordance with the terms of this Agreement for the full period provided for in Section 7.9.

Section 7.8 Equitable Remedies . Since unauthorized use or disclosure of a Discloser's Confidential Information will diminish the value to the Discloser of its proprietary interests in the Confidential Information, if the Recipient breaches any of its obligations under this Artic le 7, the Discloser shall be entitled to equitable relief to protect its interests therein, including, but not limited to, injunctive relief, as well as money damages.

Section 7.9 Confidentiality Obligations Survival . With respect to each item of Confidential Information transferred under this Agreement, the provisions of this Article 7 shall remain in effect until such time as the Recipient can demonstrate, using only legally admissible

evidence, that such item of Confidential Information is publicly known or was made generally available through no action or inaction of the Recipient.

ARTICLE 8
LIMITATION OF LIABILITY; NO WARRANTY

Section 8.1 LIMITATION ON LIABILITY . IN NO EVENT WILL EITHER PARTY'S LIABILITY IN CONNECTION WITH THIS AGREEMENT EXCEED $25,000. THIS LIMITATION APPLIES TO ALL CAUSES OF ACTION IN THE AGGREGATE, INCLUDING, WITHOUT LIMITATION, BREACH OF CONTRACT, BREACH OF WARRANTY, NEGLIGENCE, STRICT LIABILITY. MISREPRESENTATION AND OTHER TORTS.

Section 8.2 LIMITATION ON DAMAGES . IN NO EVENT WILL EITHER PARTY HAVE ANY LIABILITY TO THE OTHER PARTY FOR ANY INDIRECT, INCIDENTAL, SPECIAL, EXEMPLARY OR CONSEQUENTIAL DAMAGES ARISING OUT OF OR RELATED TO THIS AGREEMENT, HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETHER FOR BREACH OF CONTRACT, TORT OR OTHER WISE, INCLUDING BUT NOT LIMITED TO, LOSS OF ANTICIPATED PROFITS, LOSS OF DATA OR LOSS OF USE, EVEN IF SUCH PARTY HAS BEEN ADVISED OF-THE POSSIBILITY OF SUCH DAMAGES.

Section 8.3 DISCLAIMER OF WARRANTIES . ALL INSMED U.S. AND INSMED IRELAND INTANGIBLE PROPERTY RIGHTS ARE PROVIDED "AS IS" AND WITHOUT ANY WARRANTY, EXPRESS, IMPLIED OR OTHERWISE, REGARDING THEIR ACCURACY OR PERFORMANCE, AND INSMED U.S. EXPRESSLY DISCLAIMS ANY WARRANTY OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE OR NON-INFRINGEMENT.

Section 8.4 Representation and Warranty . Each Party represents and warrants to the other Party that all Developed Intangible Property Rights will not, to the best of each respective Party's knowledge, infringe any patents, copyrights, trade secret rights, trademark or trade dress rights or any other proprietary rights (including but not limited to moral rights or rights of privacy or publicity) of any Third Party, worldwide. If either Party incorporates an y technology or other Intangible property right owned by a Third Party into any Developed Technology or Developed Marketing Intangible, such Party will identify all such Third Party rights and will obtain an assignment, license or written waiver and agreement from such Third Party as necessary for such Party to comply with its obligations under this Section 8.4.

ARTICLE 9
TERM AND TERMINATION

Section 9.1 Term . This Agreement shall enter into effect on the Effective Date and shall remain in full force and effect until terminated by a written agreement between the Parties, unless terminated in accordance with Section 9.2, Section 9.3 or Section 9.4.

Section 9.2 Termination for Convenience . This Agreement may be terminated by either Party, for any reason, by giving the other Party written notice of the termination sixty (60) days in advance.

Section 9.3 Termination for Cause . This Agreement may be terminated by either Party (" **Non-Breaching Party** "), if the other Party (" **Breaching Party** ") is in material breach of this Agreement and fails to cure such breach within thirty (30) days following receipt of notice of such breach. In the event that Breaching Party fails to cure such breach or default with in thirty (30) days after the date of Non-Breaching Party's notice hereunder, Non-Breaching Party may terminate this Agreement immediately upon providing written notice of termination to Breaching Party. Termination of this Agreement in accordance with this Section 9.3 shall not affect or impair Non Breaching Party's right to pursue any legal remedy, including the right to recover damages, for all harm suffered or incurred as a result of Breaching Party's breach or default.

Section 9.4 Change in Control or Substantial Encumbrance . In the event that the Parties cease to be Affiliates, either Party undergoes an involuntary change in control or a substantial portion of either Party's assets or the conduct of either Party's business is substantially encumbered by extraordinary governmental action or by operation of Jaw, either Party may, at its opt ion and in its sole discretion, terminate this Agreement, effective immediately upon giving written notice of termination to the other Party. For purposes of this Section 9.4, notice shall be effective when sent.

Section 9.5 Effect of Termination . Upon any termination of this Agreement:

(a) the Parties shall retain the rights in the Developed Intangible Property Rights as set forth in this Agreement, including Section 5.1 and Section 5.2; and

(b) if such termination is pursuant to Section 9.3, the Breaching Party shall promptly comply with the provisions of Section 7.7.

Section 9.6 Final Payment . Upon any termination, treating the date of termination as the final Fiscal Year End, the Parties shall prepare a final Annual CSA Report as provided in Article 3 and shall arrange to pay or otherwise settle the Annual Payment Amount within sixty (60) days of termination or as provided by Section 4.1, Section 4.3, Section 4.4 and Section 4.6.

Section 9.7 Survival . In the event of the termination of this Agreement for any reason whatsoever, Article 1, Article 3, Article 4, Article 5, Article 7, Article 8 and Article 10, and Section 9.5, Section 9.6 and this Section 9.7 of this Agreement shall survive for as long as necessary to effectuate their purposes and shall bind the Parties and their Affiliates. The termination of this Agreement shall not relieve either Party of any liability under this Agreement that accrued prior to such termination.

Section 9.8 Modification . Pursuant to U.S. Treas. Reg. Sec. 1.482-7(f), in the event of a "change in participation" as defined therein, this Agreement shall be modified and arm's length consideration shall be due as provided therein.

ARTICLE 10
GENERAL PROVISIONS

Section 10.1 Assignment . Neither Party may assign this Agreement, its rights or its responsibilities hereunder without the other Party's prior written authorization. Any assignment in derogation of the foregoing shall be void.

Section 10.2 Notices . Any notice required or permitted to be given under this Agreement shall be given to the other Party either 1) in writing and delivered by overnight courier (signature of receipt required) and shall be deemed delivered upon written confirmation of delivery by the courier or 2) via e-m ail, and shall be deemed delivered provided no transmission error was received (if by email), if sent to the following respective addresses or such new addresses as may from time to time be supplied hereunder:

IF TO Insmed U.S.:
10 Finderne Avenue, Building 10,
Bridgewater, New Jersey

Attention: General Counsel
E-mail: generalcounsel@insmed.com

IF TO Insmed Ireland:
25-28 North Wall Quay
Dublin 1, Ireland

Attention: Nickola Murphy /Geraldine Lillis
E-mail: Nickola.Murphy@canyoncts.com /
Geraldine.Lillis@canyoncts.com

Section 10.3 Force Majeure . Neither Party shall be liable to the other Party for failure or delay in the performance of any obligations under this Agreement, other than the obligation to pay monies (" **Excused Obligation** "), for the time and to the extent such failure or delay is due to any cause or condition beyond the reasonable control of the Party obliged to perform, including, but not limited to, strikes or other labor difficulties. acts of God, earthquakes, acts of government (in particular with respect to the refusal to issue necessary import or export licenses), war, terrorism, riots, embargoes or inability to obtain supplies (collectively " **Force Majeure** "). If Force Majeure prevents or delays the performance by a Party hereto of any Excused Obligation under this Agreement, the Party claiming Force Majeure shall promptly notify the affected Party thereof in writing.

Section 10.4 Successors and Assigns . This Agreement shall be binding on and shall inure to the benefit of the Parties, Affiliates, their respective successors, successors in title, and assigns, and each Party agrees, on behalf of it, its Affiliates, successors, successors in tit le, and assigns, to execute any instruments that may be necessary or appropriate to carry out and execute the purpose and intentions of this Agreement and hereby authorizes and directs its Affiliates, successors, successors in title, an d assigns to execute any and all such instruments. Each and every successor in interest to any Party or Affiliate, whether such successor acquires such interest by way of gift, devise, assignment, purchase, conveyance, pledge, hypothecation, foreclosure, or by any other method, shall hold such interest subject to all of the terms and provisions of this Agreement. The rights of the Parties, Affiliates, and their successors in interest, as

among themselves and shall be governed by the terms of this Agreement, and the right of any Party, Affiliate or successor in interest to assign, sell or otherwise transfer or deal with its interests under this Agreement shall be subject to the limitations and restrictions of this Agreement.

Section 10.5 Amendment . This Agreement may only be amended or supplemented by additional written agreements or instruments specifically referencing this Agreement and signed by the Parties.

Section 10.6 Remedies Cumulative . A Party's remedies under this Agreement are cumulative and shall not exclude any other remedy to which the Party may be entitled. Termination of this Agreement by a Party shall not adversely affect or impair such Party's right to pursue any other remedy including, without limitation, the right to recover damages for all harm suffered as a result the other Party's breach or default.

Section 10.7 Further Assurances . Each Party hereby covenants and agrees that it shall execute and deliver such deeds and other documents as may be required to implement any of the provisions of this Agreement.

Section 10.8 No Waiver . The failure of any Party to insist on strict performance of a covenant hereunder or of any obligation hereunder shall not be a waiver of such Party's right to demand strict compliance therewith in the future, nor shall the same be construed as a novation of this Agreement.

Section 10.9 Entire Agreement . This Agreement (including its Exhibits and any amendments) contains the entire agreement of the Parties with respect to the subject matter of this Agreement, except for agreements referenced in this Agreement, and supersedes all previous communications, representations, understandings and agreements, either oral or written, between the Parties with respect to the subject matter hereof.

Section 10.10 Headings; Construction . The headings in this Agreement are for convenience only and will not be construed to affect the meaning of any provision of this Agreement. Any use of "including" shall also be deemed to mean "including without limitation."

Section 10.11 Number and Gender . Whenever required by the context, the singular number shall include the plural, the plural number shall include the singular, and the gender of any pronoun shall include all genders.

Section 10.12 Counterparts . This Agreement may be executed in multiple copies, each of which shall for all purposes constitute an Agreement, binding on the Parties, and each Party hereby covenants and agrees to execute all duplicates or replacement counterparts of this Agreement as may be required.

Section 10.13 Governing Law and Jurisdiction . Any questions, claims, disputes or litigation concerning or arising from this Agreement shall be governed by the laws of the State of New Jersey, United States of America, without giving effect to the conflicts of laws principles of that state or doctrines of any other state of the United States, or any nation state. Each of the Parties agrees to submit to the exclusive jurisdiction of the courts in the State of New Jersey and the United States Federal courts, for any matter arising out of or relating to this Agreement Notwithstanding the foregoing, in actions seeking to enforce any order or any judgment of any such courts located in State of New Jersey, personal jurisdiction shall be non-exclusive. The Parties agree that the United Nations Convention on Contracts for the International Sale of Goods is specifically excluded from application to this Agreement.

Section 10.14 Computation of Time . Whenever the last day for the exercise of any privilege or the discharge of any duty hereunder shall fall on a Saturday, Sunday or any public or legal holiday, whether local or national, the person having such privilege or duty shall have until 5:00 p.m. on the next succeeding business day to exercise such privilege, or to discharge such duty.

Section 10.15 Severability . I n the event any provision, clause, sentence, phrase, or word hereof, or the application thereof in any circumstances, is held to be invalid or unenforceable, such invalidity or unenforceability shall not affect the validity or enforceability of the remainder hereof, or of the application of any such provision, sentence, clause, phrase, or word in any other circumstances.

Section 10.16 Costs and Expenses . Unless otherwise provided in this Agreement, each Party shall bear all fees and expenses incurred in performing its obligations under this Agreement.

Section 10.17 Taxes . Each Party hereto shall be responsible for any and all taxes levied on such Party as a result of the performance of each Party's respective activities under this Agreement. To the extent any withholding taxes apply to any payment, such payment shall be made net of such withholding tax. The Parties shall cooperate to provide each other with any documentation necessary to claim a reduced rate of withholding tax under any relevant tax treaty.

Section 10.18 Authority and Compliance Under Corporate Charter . Each Party hereby warrants, represents and covenants that it is a duly organized and existing company under the respective laws of its jurisdiction of incorporation and has the full rights, power and authority pursuant to its corporate charter, articles of incorporation and /or by-laws to enter into and perform all obligations under this Agreement. Each Party further warrants, represents and covenants that in exercising any and/or all rights and in performing any and/or all obligations under this Agreement, each Party and/or its Representatives will act in full accordance with its respective corporate charter, articles of incorporation and/or by-laws.

[SIGNATURE PAGE FOLLOWS]

By their Signatures, the authorized representatives of the Parties acknowledge the Parties' acceptance of this Agreement:

Insmed Incorporated		**Insmed Ireland Limited**	
By:	/s/ Andrew Drechsler	By:	/s/ Geraldine Lillis
Name:	Andrew Drechsler	Name:	Geraldine Lillis
Title:	Chief Financial Officer	Title:	Director
Date:	May 28, 2015	Date:	May 29, 2015

Schedule 3

PLATFORM CONTRIBUTION TRANSACTION ("PCT")
INTANGIBLE PROPERTY LICENSE AGREEMENT

INSMED INCORPORATED - INSMED IRELAND LIMITED

This PLATFORM CONTRIBUTION TRANSACTION INTANGIBLE PROPERTY LICENSE AGREEMENT ("Agreement"), effective as of April 1, 2015 is by and between Insmed Ireland Limited ("Insmed Ireland"), a limited liability company organized under the laws of Ireland, with registered office at 25-28 North Wall Quay, Dublin l, Ireland, registered with the Registrar of Companies under number 550604 and Insmed Incorporated ("Insmed U.S."), a corporation organized under the laws of Virginia with principal place of business at 10 Finderne Avenue, Building 10, Bridgewater. New Jersey (collectively, the "Parties" and individually, "Party").

RECITALS

WHEREAS , Insmed U.S. is engaged, directly or through its subsidiaries, affiliates, sub contractors, contract developers or licensors, in the business of researching, developing, marketing and distributing pharmaceuticals products (collectively, the "Products" as further defined below) and has developed certain intangibles related to said Products;

WHEREAS , Insmed U.S. is currently the owner or licensee of legal and beneficial rights to specific products and intangibles (as defined in Section 1.5);

WHEREAS , the Parties have entered into the certain Cost Sharing Agreement effective as of April l, 2015, a qualified cost sharing arrangement in accordance with U.S. Treasury Regulations § 1.482-7 (the "CSA"), to pool their resources for the purpose of developing and otherwise enhancing the value of future intangibles and to share the benefits therefrom;

WHEREAS , in conjunction with the CSA, Insmed Ireland desires to obtain from Insmed U.S. a license to certain pre-existing rights and platform contributions (collectively "Intangibles", as further defined in Section 1.5) in its Field of Use (as defined in Section 1.3);

WHEREAS , the Parties des ire to use their respective Intangible Property Rights to develop technologies. products and to further enhance their intangible right s with respect to the Parties· respective Field of Use; and

WHEREAS , Insmed U.S. is willing to grant a non-exclusive right to exercise certain product technologies and intangible property rights under the aforementioned license within Insmed Ireland's Field of Use, and Insmed Ireland is willing to accept such rights and obligations.

NOW, THEREFORE , in consideration of the mutual covenants and conditions contained herein and intending to be legally bound, the Parties hereby agree as follows:

ARTICLE 1
DEFINITIONS

Section 1.1 " **Affiliate** " or " **Affiliates** " of a Party means any entity controlled by, controlling or under common control with such Party, where "control" in any of the foregoing forms means ownership, either direct or indirect. of more than fifty percent (50%) of the equity interest entitled to vote for the election of directors or equivalent governing body. An entity shall be considered an Affiliate only so long as such entity continues to meet the foregoing definition.

Section 1.2 " **Effective Date** " means April 1, 2015.

Section 1.3 " **Field of Use** " means customers and business operations located outside of the United States of America for Insmed Ireland and customers and business operations located in the United States of America for Insmed U.S.

Section 1.4 " **Fiscal Year** " means the period from January 1 to December 31 of each year.

Section 1.5 " **Intangibles** " or " **Intangible Property Rights** " means any and all rights of any kind, including intellectual property rights, existing whether or not registered and all applications, renewals, extensions of the same and whenever arising, registered or applied to be registered, arising before the Effective Date that Insmed U.S. presently owns or has the right to license to Insmed Ireland, Affiliates, assignees and/or licensees (by whatever name or term known or designated) related to the Products outlined in Exhibit A, including, without limitation:

(a) all inventions, know-how, technical data, trade secrets, functional or detailed design specifications, designs and enhancements, whether patentable or un-patentable, patented or un-patented;

(b) all trademarks, copyrights, service marks and trade name rights, internet domain names, social media designations, and other designations and similar rights;

(c) all franchises, licenses, or contracts;

(d) all rights associated with works of authorship throughout the world, including but not limited to copyrights, moral rights and software;

(e) all Patents (including provisionals, continuations, continuations-in-part, and divisionals thereof), reissues and re-examinations thereof, database rights, design rights and other industrial property rights that have the benefit of a filing date on or after the Effective Date;

(f) all patent applications (including continuations, continuations-in-part and divisionals thereof) now or hereafter in force, that have the benefit of a filing date on or after the Effective Date;

(g) all rights, including copyrights. Confidential Information and trade secrets underlying the technology and any prints, packaging, labels, advertising or promotional material and any other materials of any kind using or used in conjunction with trademarks and know-how underlying the developed marketing intangibles, whether created by the Parties their Affiliates or any Third Party engaged by the Parties or their Affiliates to create any thereof; and

(h) any additional applicable intangible property as defined under U.S. Treas. Reg. Sec. 1.482-4(b) (whether or not in documentary form and whether or not patentable, copyrightable, or otherwise protectable under applicable laws).

Section 1.6 " **Revenues** " means the gross revenues determined in accordance with U.S. Generally Accepted Accounting Principles ("GAAP") for financial reporting purposes and shall mean the revenues recognized by or for the account of Insmed Ireland from the sale or license of the Products and any related services. provided that Revenues shall not include any of the following:

(a) Any government taxes or levies collected from customers with respect to the sale of or the license relating to the Products that are to be paid over to any applicable governmental authority: or

(b) Any amounts associated with the shipment and delivery of the Products, including, without limitation, all freight charges, freight forwarding fees. customs fees and insurance premiums; or

(c) Any portion of the sales or license revenues of the Products that is refunded to a customer; or

(d) Any revenues received from an Affiliate.

Section 1.7 " **Sublicensee** " means a license entered into by Insmed Ireland in accordance with Section 2.2 of Artic le 2 of this Agreement.

Section 1.8 " **Sub-contractor** " means an affiliate or unrelated party, under an agreement. as a sub-contractor, undisclosed agent, commissionaire, or similar party, acting on behalf of one of the Parties.

Section 1.9 " **Third Party** " **or** " **Third Parties** " means any entity other than a Party to this Agreement or an Affiliate of the Parties.

ARTICLE 2
GRANT OF RIGHT TO USE INTANGIBLES AND INTANGIBLE PROPERTY RIGHTS

Section 2.1 License of Rights . Subject to the terms and conditions of this Agreement and unless otherwise mutually agreed to by the Parties in writing, as of the Effective Date. Insmed U.S. hereby grants to Insmed Ireland a non-exclusive. perpetual right and license in and to the Intangibles within its Field of Use to make, have made, use, sell, offer to sell, perform, display, reproduce, and distribute the Products and to make improvements, modifications and/or enhancements to the intangibles.

Section 2.2 Licenses from Third Parties . The license granted under Section 2.1 (License of Rights) includes all economic rights and licenses granted to the Parties by Third Parties to the extent those rights relate to the development and/or use of the Products and may be sublicensed to the Parties.

Section 2.3 Right to Sublicense . Insmed Ireland shall have the right to sublicense to Third Parties the rights licensed to Insmed Ireland pursuant to Section 2.1 (License of Rights).

Section 2.4 Quality . Sales by Insmed Ireland (or a Sublicensee or Sub-contractor) shall meet the quality control standards and specifications established from time-to-time by Insmed U.S., including any requirements of applicable regulatory agencies in the Parties' respective Field of Use. Insmed U.S. shall have the right, at its expense, to audit Insmed Ireland's quality control of Sales from time-to-time on a reasonable basis and on reasonable prior notice to Insmed Ireland. In the event that quality control of Insmed Ireland (or a Sublicensee or a Sub-contractor) falls below Insmed U.S.'s standards and specifications, Insmed U.S. shall give Insmed Ireland written notice of such failures, and Insmed Ireland shall, at its expense and within the reasonable notice period set out in the notice, take such corrective action as is necessary to restore quality to the appropriate level.

ARTICLE 3
PAYMENT

Section 3.1 Compensation . Subject to this Article 3 and consideration for the license granted to Insmed Ireland under this Agreement, Insmed Ireland agrees to make a PCT Payment to Insmed U.S. that produces an arm's length result, as provided in Exhibit B .

Section 3.2 Timing and Manner of Payments . The PCT Payments shall be payable and due as outlined in Exhibit B through the final date, on which date all such PCT amounts shall be fully paid.

Section 3.3 Pre-Payment Option . The Patties agree that Insmed Ireland has the option, without penalty, to pre-pay the PCT Payments, in whole or in part, during the term of this Agreement, but in no event prior to 2016. Any pre-payment amount shall reduce the net present value of the outstanding payments still remaining under Section 3.1 (Compensation). Upon such pre payment. if any, the net present value of the outstanding future PCT Payments shall be calculated using a discount rate that is reflective of the then current risk associated with the forecasted Bookings. Upon such pre-payment, the Parties will mutually develop a new schedule for payment of the remaining amounts due, if any, under this Agreement.

Section 3.4 Manner of Payment . A netting of any amount payable under this Agreement as against existing accounts payable and accounts receivable shall be acceptable payment, effective as of the date of the netting on the books of the Parties.

Section 3.5 Currency . All royalties contemplated hereby shall be made in U.S. Dollars or in a currency as mutually agreed to by the Parties. Any reported amount in currencies other than the U.S. Dollars shall be translated into U.S. Dollars at the prevailing bookkeeping

rate used by the Parties during the period in which the amount is recognized under U.S. GAAP as applied for financial reporting purposes.

Section 3.6 Withholding Taxes and Related Matters . Any withholding or related tax or other obligations relating to the payments due under the terms of this Agreement shall be complied with by Insmed Ireland. and shall not alter the amount of the obligation of Insmed Ireland under this Article 3.

Section 3.7 Revenues Data . Insmed Ireland shall maintain complete and accurate records of all Revenues. Insmed U.S. shall have the right, at its expense and on a reasonable basis with reasonable prior written notice to Insmed Ireland, to examine such records during regular business hours during the term of this Agreement and for 6 months after termination of this Agreement.

ARTICLE 4
CONFIDENTIAL INFORMATION

Section 4.1 Definition of Confidential Information . The Parties acknowledge that from time to time, one Party (the "Discloser") may disclose to the other Party (the "Recipient") information: (a) that is marked with "confidential" or a similar legend; or (b) that is described orally and designated as confidential; or (c) that would, under the circumstances, be understood by a reasonable person to be confidential ("Confidential Information"). Any unmarked or oral information conveyed during a meeting between employees of the Parties discussing Confidential Information will be Confidential Information by default whether or not declared confidential and whether or not it is subsequently described in writing. Upon subsequent disclosure of previously disclosed Confidential Information to the Recipient by the Discloser, the information will remain Confidential Information even if not identified as confidential information at the subsequent disclosure. The Intangibles shall be considered Confidential Information of the Parties.

Section 4.2 Confidentiality Obligations . The Recipient shall retain such Confidential Information in confidence, and shall not disclose it to any Third Party or use it for other than the purposes of this Agreement without the Discloser's prior written consent, unless disclosure is made to the Recipient's professional consultants who are bound to confidentiality under their professional law (e.g. lawyers, tax advisers and auditors) excluding Securities Exchange Commission ("SEC") filings and investor presentations. Each Party shall use at least the same procedures and degree of care with respect to such Confidential Information that it uses to protect its own confidential information of like importance, and in no event less than reasonable care. The Recipient will immediately give written notice to the Discloser of any unauthorized use or disclosure of the Discloser's Confidential Information, and the Recipient will assist the Discloser in remedying such unauthorized use or disclosure.

Section 4.3 Compelled Disclosure . In the event that the Recipient or (to the knowledge of the Recipient) any of its Representatives is requested or required (by oral questions, interrogatories, requests for information or documents in legal proceedings, subpoenas, civil investigative demands or other similar processes) to disclose any of the Discloser's Confidential Information, the Recipient shall, unless legally prohibited, provide the

Discloser with prompt written notice of any such request or requirement sufficiently timely to allow the Discloser adequate time to seek a protective order or other appropriate remedy and/or waive compliance with the provisions of this Agreement. If, in the absence of a protective order or other remedy, or where applicable law or regulation does not permit Recipient to provide such notice, or in the event of the receipt of a waiver by the Discloser, the Recipient or any of its representatives are, upon the advice of counsel, required to disclose the Confidential Information to any tribunal or regulatory authority, or stand liable for contempt or suffer other censure or penalty, the Recipient or any of its representatives may, without liability hereunder, disclose to such tribunal only that portion of the Confidential Information which such counsel advises the Recipient that it is required to disclose; provided, that the Recipient exercises its best efforts to preserve the confidentiality of the Confidential Information, including, without limitation, by cooperating, to the extent permissible by applicable law or regulation, with the Discloser in the Discloser's efforts to obtain an appropriate protective order or other reliable assurance that confidential treatment will be accorded the Confidential Information by such tribunal or regulatory authority.

Section 4.4 Exceptions . Notwithstanding the foregoing, Confidential Information will not include certain information to the extent such information:

(a) was generally available to the public at the time of its disclosure to the Recipient hereunder;

(b) became generally available to the public after its disclosure other than through an act or omission of the Recipient (or one of its employees, agents or Representatives) in breach of this Agreement; or

(c) was subsequently lawfully and independently disclosed to the Recipient by a person other than the Discloser without an obligation of confidentiality.

Section 4.5 Contractors . Prior to the Recipient's disclosure of any of the Discloser's Confidential Information to any Third Party for which the Recipient has obtained the Discloser's prior consent, the Recipient must require the Third Party to enter into a nondisclosure agreement ("NDA") provided by the Discloser, the terms of which NDA will take precedence over the Third Party agreement.

Section 4.6 Ownership of Materials . Each Recipient agrees that all Confidential Information received is and will remain the property of the Discloser and that such shall not be copied or reproduced without the express permission of the Discloser, except for such copies as may be reasonably necessary in order to accomplish the purpose of this Agreement. Upon written request of the Discloser, the Recipient shall immediately discontinue all use of all Confidential In formation of the Discloser and shall, at the Discloser's option, either destroy or return to the Discloser all hard copies in its possession of such Confidential Information and any derivatives thereof (including all hard copies of any translation, modification, compilation, abridgement or other form in which the Confidential Information has been recast, transformed or adapted), and to delete all electronic copies thereof; provided, however, that the Recipient may retain one (1) archival copy of the Confidential Information, which shall be used only in case of a dispute concerning this Agreement. Notwithstanding the

foregoing, neither Party shall be required to destroy or alter any computer-based back-up files generated in the normal course of its business, provided that such files are maintained confidential in accordance with the terms of this Agreement for the full period provided for in Section 4.8 (Confidentiality Obligations Survival).

Section 4.7 Equitable Remedies . Since unauthorized use or disclosure of the Discloser's Confidential Information will diminish the value to the Discloser of its proprietary interests in the Confidential Information, if the Recipient breaches any of its obligations under this Article 4, the Discloser shall be entitled to equitable relief to protect its interests therein, including, but not limited to, injunctive relief, as well as money damages.

Section 4.8 Confidentiality Obligations Survival . With respect to each item of Confidential Information transferred under this Agreement, the provisions of this Article 4 shall remain in effect until such time as the Recipient can demonstrate, using only legally admissible evidence, that such item of Confidential Information is publicly known or was made generally available through no action or inaction of the Recipient.

ARTICLE 5
WARRANTIES AND REPRESENTATIONS AND DISCLAIMERS

Section 5.1 Warranties . Each of the Parties hereby represents and warrants to the other as of the Effective Date that: (i) it is a company duly organized, validly existing, and in good standing under the laws of the jurisdiction of organization, and has full corporate power and authority to enter into this Agreement; (ii) this Agreement has been duly executed and delivered by it and is a binding obligation of it, enforceable in accordance with its terms, subject, as to enforcement of remedies, to applicable bankruptcy, insolvency, moratorium, reorganization, and similar laws affecting creditors' rights generally, and to general equitable principles; (iii) it is not subject to a pet it ion for relief under any bankruptcy legislation, it has not made an assignment for the benefit of creditors, it is not subject to the appointment of a receiver for all or a substantial part of its assets, and it is not contemplating taking or becoming subject to any of the foregoing; and (iv) it is in compliance, and has complied, with all applicable laws and regulations (including labor laws and tax laws).

Section 5.2 Disclaimers . EXCEPT FOR THE EXPRESS WARRANTIES SET FORTH IN SECTION 6.1 (WARRANTIES), EACH PARTY MAKES NO REPRESENTATIONS OR WARRANTIES UNDER THIS AGREEMENT AND DISCLAIMS ALL IMPLIED REPRESENTATIONS AND WARRANTIES, INCLUDING ANY IMPLIED WARRANTIES OF MERCHANTABILITY. FITNESS FOR A PARTICULAR PURPOSE, TITLE, AND NONINFRINGEMENT. THE INTANGIBLES PROVIDED UNDER THIS AGREEMENT ARE "AS IS" AND MAY CONTAIN DEFICIENCIES, AND INSMED U.S. MAKES NO REPRESENTATIONS OR WARRANTIES UNDER THIS AGREEMENT REGARDING THE USE OR PERFORMANCE OF SUCH INTANGIBLES.

Section 5.3 Limitation on Liability . IN NO EVENT WILL INSMED U.S. HAVE ANY LIABILITY FOR ANY INDIRECT, INCIDENTAL, SPECIAL, EXEMPLARY, OR CONSEQUENTIAL DAMAGES, HOWEVER CAUSED AND ON ANY THEORY OF LIABILITY, WHETHER FOR BREACH OF CONTRACT, TORT OR OTHERWISE,

ARISING OUT OF OR RELATED TO THIS AGREEMENT, INCLUDING BUT NOT LIMITED TO, LOSS OF ANTICIPATED PROFITS, LOSS OF DATA, OR LOSS OF USE, EVEN IF INSMED U.S. HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

Section 5.4 No Damages for Termination or Expiration . Neither Party shall be liable to the other for damages of any kind, including incidental or consequential damages, or arising from any expenditure, investment, lease or other commitment, on account of the termination or expiration of this Agreement in accordance with its terms. Each Party waives any right it may have to receive any compensation or reparations on termination or expiration of this Agreement in accordance with the terms of this Agreement not including any payment obligations, and notwithstanding, the law of any territory or otherwise. Each Party acknowledges that they will not have or acquire by virtue of this Agreement or otherwise any vested, proprietary or other right in the "goodwill" of the other Party's trademarks or service marks.

ARTICLE 6
INDEMNIFICATION

Section 6.1 Indemnification by Insmed U.S . Insmed U.S. shall defend, indemnify and hold harmless Insmed Ireland from and against any claims, demands, causes of actions, liabilities, damages, losses, costs, liabilities or expenses of any kind, including reasonable attorneys' fees (collectively, "Claims") arising from (i) actual or alleged infringement or misappropriation of any third party patent, trademark, copyright, trade secret or other intellectual property right held by a third party (unless such actual or alleged infringement arises from Intangible Property Rights owned by Insmed Ireland or subsequently developed by Insmed Ireland), (ii) Insmed U.S.'s gross negligence, willful misconduct and/or violation of applicable laws or regulations, and/or (iii) Insmed U.S.'s breach of any of its representations or warranties unless gross negligence or willful misconduct of Insmed Ireland. Insmed U.S. shall defend any such claim or action at its own expense provided that Insmed Ireland promptly notifies Insmed U.S. upon learning of such Claim, provides Insmed U.S. with sole control of the defense and settlement of any such Claim, and cooperates with Insmed U.S. in defending any such Claim.

Section 6.2 Indemnification by Insmed Ireland . Insmed Ireland shall defend, indemnify and hold harmless Insmed U.S. from and against any Claims arising from (i) actual or alleged infringement or misappropriation of any third party patent, trademark, copyright, trade secret or other intellectual property right held by a third party (unless such actual or alleged infringement arises from Intangible Property Rights owned by Insmed U.S. or subsequently developed by Insmed U.S.), (ii) Insmed Ireland's gross negligence, willful misconduct and/or violation of applicable laws or regulations, and/or (iii) Insmed Ireland's breach of any of its representations or warranties unless gross negligence or willful misconduct of Insmed U.S. Insmed Ireland shall defend any such claim or action at its own expense provided that Insmed U.S. promptly notifies Insmed Ireland upon teaming of such Claim, provides Insmed Ireland with sole control of the defense and settlement of any such Claim, and cooperates with Insmed Ireland in defending any such Claim.

ARTICLE 7
INTANGIBLES OWNERSHIP

Section 7.1 Retention of Legal Title . Except for the license grants expressly provided in t h is Agreement, all rights, title and interests in and to the Intangibles, whether made by Insmed U.S., Insmed Ireland, or its Sublicensees ("Rights and Technology"), is and shall at al l times remain with Insmed U.S. Insmed Ireland and /or its Sublicensees shall not at any time during or after the expiration or termination of this Agreement in any way question or dispute the ownership thereof by Insmed U.S. For purposes of clarity, unless otherwise specified in this Agreement, Insmed U.S. holds the following rights, which Insmed U.S. may exercise in its sole discretion: (i) the right to control the quality standard relative to the Intangibles; (ii) the right to apply for and obtain registrations for the Intangibles; (ii i) the right to enforce the Intangibles against Third Parties; (iv) the right to defend Third Party objections to or claims against the Intangibles; and (v) the right to maintain and abandon the applications, registrations, and other statutory rights in and to the Intangibles. In addition, Insmed U.S. covenants to maintain (at its own expense) the existing registrations and legal protections in respect of the Intangibles throughout the term of this Agreement. For purposes of interpretation of this Section under the Lanham (Trademark) Act and all other applicable trademark laws or regulations, all goodwill arising from the use of the Intangibles will inure to the benefit of Insured U.S. Subject to the rights licensed to Insmed Ireland in this Agreement, Insmed Ireland and/or its Sublicensees hereby assigns to Insmed U.S. any and all rights, title and interest i t may have or acquire in such Rights and Technology, and will execute and provide to Insmed U.S. all documents and instruments of conveyance respecting the foregoing Rights and Technology as may be appropriate to perfect Insmed U.S.'s legal title thereto. The absence of such documents and instruments of conveyance shall not limit the rights of Insmed U.S. in the foregoing Rights and Technology. To the extent any of the rights, title and interest in and to the Rights and Technology cannot be assigned by Insmed Ireland and/or its Sublicensees to Insmed U.S., Insmed Ireland and/or its Sublicensees hereby grant to Insmed U.S. an exclusive, royalty-free, transferable, perpetual, unrestricted, worldwide license (with rights to sublicense through one or more tiers of Sublicensees) to any non-assignable Rights and Technology. To the extent any of such Rights and Technology can be neither assigned nor licensed by Insmed Ireland and/or its Sublicensees to Insmed U.S., Insmed Ireland and/or its Sublicensees hereby waives and agrees never to assert such nonassignable and non-licensable Rights and Technology against Insmed U.S., Insmed U.S.'s Affiliates, Insmed U.S.'s licensees or Insmed U.S.'s successors, or its and their respective customers.

ARTICLE 8
TERM AND TERMINATION

Section 8.1 Term . This Agreement shall enter into effect on the Effective Date and shall remain in full force and effect until terminated by a written agreement between the Parties, unless terminated in accordance with Section 8.2, Section 8.3 or Section 8.4.

Section 8.2 Termination for Convenience . This Agreement may be terminated by either Party, for any reason, by giving the other Party written notice of the termination sixty (60) days in advance.

Section 8.3 Termination for Cause . This Agreement may be terminated by either Party (" **Non-Breaching Party** "), if the other Party (" **Breaching Party** ") is in material breach of this Agreement and fails to cure such breach within thirty (30) days following receipt of notice of such breach. In the event that Breaching Party fails to cure such breach or default within thirty (30) days after the date of Non-Breaching Party's notice hereunder, Non-Breaching Party may terminate this Agreement immediately upon providing written notice of termination to Breaching Party. Termination of this Agreement in accordance with this Section 8.3 shall not affect or impair Non Breaching Party's right to pursue any legal remedy, including the right to recover damages, for all harm suffered or incurred as a result of Breaching Party's breach or default.

Section 8.4 Change in Control or Substantial Encumbrance . In the event that the Parties cease to be Affiliates, either Party undergoes an involuntary change in control or a substantial portion of either Party's assets or the conduct of either Party's business is substantially encumbered by extraordinary governmental action or by operation of law, either Party may, at its option and in its sole discretion, terminate this Agreement, effective immediately upon giving written notice of termination to the other Party. For purposes of this Section 8.4, notice shall be effective when sent.

Section 8.5 Effect of Termination . Upon any termination of this Agreement, Insmed U.S. shall have the right to retain any sums already paid by Insmed Ireland under this Agreement, and Insmed Ireland shall pay all sums accrued that are then due under this Agreement. Further, Insmed Ireland shall immediately cease to exercise all use of the Intangibles and shall have no further right, title, or interest i n any trademark or other valuable intangible property right under this agreement other than the rights obtained under the Cost Sharing Agreement entered into by the parties.

Section 8.6 Modification . Pursuant to U.S. Treas. Reg. Sec. 1.482-7(f), in the event of a "change in participation" as defined therein, this Agreement shall be modified and arm's length consideration shall be due as provided therein.

ARTICLE 9
GENERAL PROVISIONS

Section 9.1 Assignment . Neither Party may assign this Agreement, its rights, or responsibilities hereunder without the prior written authorization of the other Party. Any assignment in derogation of the foregoing shall be void.

Section 9.2 Notices . Any notice required or permitted to be given under this Agreement shall be given to the other Party either 1) in writing and delivered by overnight courier (signature of receipt required) and shall be deemed delivered upon written confirmation of delivery by the courier or 2) via e-mail, and shall be deemed delivered provided no transmission error was received (if by e-mail), if sent to the following respective addresses or such new addresses as may from time to time be supplied hereunder:

IF TO Insmed U.S.:
10 Finderne Avenue, Building 10,
Bridgewater, New Jersey

Attention: General Counsel
E-mail: generalcounsel@insmed.com

IF TO Insmed Ireland:
25-28 North Wall Quay
Dublin 1, Ireland

Attention: Nickola Murphy/Geraldine Lillis
E-mail: Nickola.Murphy@canyoncts.com /
Geraldine.Lillis@canyoncts.com

Section 9.3 Force Majeure . Neither Party shall be liable to the other Party for failure or delay in the performance of any obligations under this Agreement. other than the obligation to pay monies (" **Excused Obligation** "), for the time and to the extent such failure or delay is due to any cause or condition beyond the reasonable control of the Party obliged to perform, including, but not limited to, strikes or other labor difficulties, acts of God, earthquakes, acts of government (in particular with respect to the refusal to issue necessary import or export licenses), war, terrorism, riots, embargoes or in ability to obtain supplies (collectively " **Force Majeure** "). If Force Majeure prevents or delays the performance by a Party hereto of any Excused Obligation under this Agreement, the Party claiming Force Majeure shall promptly notify the affected Party thereof in writing.

Section 9.4 Successors and Assigns . This Agreement shall be binding on and shall inure to the benefit of the Parties, Affiliates, their respective successors, successors in title, and assigns, and each Party agrees, on behalf of it, its Affiliates. successors, successors in title, and assigns, to execute any instruments that may be necessary or appropriate to carry out and execute the purpose and intentions of this Agreement and hereby authorizes and directs its Affiliates, successors, successors in title, and assigns to execute any and all such instruments. Each and every successor in interest to any Party or Affiliate, whether such successor acquires such interest by way of gift, devise, assignment, purchase, conveyance, pledge, hypothecation, foreclosure, or by any other method, shall hold such interest subject to all of the terms and provisions of this Agreement. The rights of the Parties, Affiliates, and their successors in interest, as among themselves and shall be governed by the terms of this Agreement. and the right of any Party, Affiliate or successor in interest to assign, sell or otherwise transfer or deal with its interests under this Agreement shall be subject to the limitations and restrictions of this Agreement.

Section 9.5 Amendment . This Agreement may only be amended or supplemented by additional written agreements or instruments specifically referencing this Agreement and signed by the Parties.

Section 9.6 Remedies Cumulative . A Party's remedies under this Agreement are cumulative and shall not exclude any other remedy to which the Party may be entitled. Termination of this Agreement by a Party shall not adversely affect or impair such Party's right to pursue any other remedy including, without limitation, the right to recover damages for all harm suffered as a result the other Party's breach or default.

Section 9.7 Further Assurances . Each Party hereby covenants and agrees that it shall execute and deliver such deeds and other documents as may be required to implement any of the provisions of this Agreement.

Section 9.8 No Waiver . The failure of any Party to insist on strict performance of a covenant hereunder or of any obligation hereunder shall not be a waiver of such Party's right to demand strict compliance therewith in the future, nor shall the same be construed as a novation of this Agreement.

Section 9.9 Entire Agreement . This Agreement constitutes the full and complete agreement of the Parties.

Section 9.10 Headings; Construction . The headings in this Agreement are for convenience only and will not be construed to affect the meaning of any provision of this Agreement. Any use of "including" shall also be deemed to mean "including without limitation.

Section 9.11 Number and Gender . Whenever required by the context, the singular number shall include the plural, the plural number shall include the singular, and the gender of any pronoun shall include all genders.

Section 9.12 Counterparts . This Agreement may be executed in multiple copies, each of which shall for all purposes constitute an Agreement, binding on the Parties, and each Party hereby covenants and agrees to execute all duplicates or replacement counterparts of this Agreement as may be required.

Section 9.13 Governing Law and Jurisdiction . Any questions, claims, disputes or litigation concerning or arising from this Agreement shall be governed by the laws of the State of New Jersey, United States of America, without giving effect to the conflicts of laws principles of that state or doctrines of any other state of the United States, or any nation state. Each of the Parties agrees to submit to the exclusive jurisdiction of the courts in the State of New Jersey and the United States Federal courts, for any matter arising out of or relating to this Agreement. Notwithstanding the foregoing, in actions seeking to enforce any order or any judgment of any such courts located in State of New Jersey, personal jurisdiction shall be non-exclusive. The Parties agree that the United Nations Convention on Contracts for the International Sale of Goods is specifically excluded from application to this Agreement.

Section 9.14 Computation of Time . Whenever the last day for the exercise of any privilege or the discharge of any duty hereunder shall fall on a Saturday, Sunday or any public or legal holiday, whether local or national, the person having such privilege or duty shall have until 5:00 p.m. on the next succeeding business day to exercise such privilege, or to discharge such duty.

Section 9.15 Severability . In the event any provision, clause, sentence, phrase, or word hereof, or the application thereof in any circumstances, is held to be invalid or unenforceable, such invalidity or unenforceability shall not affect the validity or enforceability of the remainder hereof, or of the application of any such provision, sentence, clause, phrase, or word in any other circumstances.

Section 9.16 Costs and Expenses . Unless otherwise provided in this Agreement, each Party shall bear all fees and expenses incurred in performing its obligations under this Agreement.

Section 9.17 Taxes . Each Party hereto shall be responsible for any and all taxes levied as a result of the performance of each Party's respective activities under this Agreement. To the extent any withholding taxes apply to any payment, such payment shall be made net of such withholding tax.

Section 9.18 Authority and Compliance Under Corporate Charter . Each Party hereby warrants, represents and covenants that it is a duly organized and existing company under the respective laws of its jurisdiction of incorporation and has the full rights, power and authority pursuant to its corporate charter, articles of incorporation and /or by-laws to enter in to and perform all obligations under this Agreement. Each Party further warrants, represents and covenants that in exercising any and/or all rights and in performing any and/or all obligations under this Agreement, each Party and/or its Representatives will act in full accordance with its respective corporate charter, articles of incorporation and/or by-laws.

[SIGNATURE PAGE FOLLOWS]

By their signatures, the authorized representatives of the Parties acknowledge the Parties' acceptance of this Agreement

INSMED IRELAND LIMITED	**INSMED INCORPORATED**
/s/ Geraldine Lillis	/s/ Andrew Drechsler
Signature	Signature
Name: Geraldine Lillis	Name: Andrew Drechsler
Title: Director	Title: Chief Financial Officer
Date: May 29, 2015	Date: May 28, 2015

EXHIBIT A

DETAIL OF PRODUCTS RELATED TO THE INTANGIBLE PROPERTY RIGHTS

Pursuant to Section 1.5, Insmed U.S. shall grant a license with respect to the Intangible Property Rights related to the patents and products associated with:

1. ARIKAYCE
2. INS-1009
3. Any other products or development currently owned by Insmed U.S. prior to the execution of this Agreement

EXHIBIT B
PAYMENTS

Pursuant to Article 3 (‘·Payment”), Insmed Ireland shall make payments in consideration for payments due under this Agreement payments in the following manner:

2015 $6,000,000 due on June 1, 2015

2016 $10.000,000 due on July 1, 2016

2017 $12,000,000 due on July l, 2017

Insmed Ireland will then make quarterly PCT payment to Insmed U.S. pursuant to Section 3.2. The payments may be based on a reasonable estimate for each quarter and trued up at the end of the year. The payments shall be made in the following manner:

2018 12% of Revenues

2019 10% of Revenues

2020 8% of Revenues

2021 4% of Revenues

All of the above payments are in conformity with the arm’s length methodologies as specified in 1.482-7(h)(2)(i)(B).

Subject to Section 3.3, Insmed Ireland reserves the right to pre-pay the remainder of the contingent payments, based on estimated Revenues as agreed by the Parties.

Exhibit 10.12.5

AMENDMENT NO. 5
TO
LOAN AND SECURITY AGREEMENT

THIS AMENDMENT NO. 5 TO LOAN AND SECURITY AGREEMENT (this ***"Amendment")*** is dated as of December 22, 2015 and is entered into by and among (a) **INSMED INCORPORATED,** a Virginia corporation ***("Parent"),*** **INSMED PHARMACEUTICALS, INC.,** a Virginia corporation ***("Insmed Pharma"),*** **CELTRIX PHARMACEUTICALS, INC.,** a Delaware corporation ***("Celtrix"),*** **TRANSAVE, LLC,** a Delaware limited liability company ***("Transave",*** together with Parent, Insmed Pharma, and Celtrix are hereinafter collectively referred to as the ***"Borrowers"*** and each individually as a ***"Borrower"),*** and (b) **HERCULES TECHNOLOGY GROWTH CAPITAL, INC.,** a Maryland corporation ***("Hercules Growth"),*** **HERCULES CAPITAL FUNDING TRUST 2012-1,** a statutory trust created and existing under the laws of the State of Delaware ***("Hercules 2012"),*** and **HERCULES CAPITAL FUNDING TRUST 2014-1,** a statutory trust created and existing under the laws of the State of Delaware ***("Hercules 2014",*** together with Hercules Growth and Hercules 2012 collectively referred to as the ***"Lender").*** Capitalized terms used herein without definition shall have the same meanings given them in the Loan Agreement (as defined below).

RECITALS

A. Borrowers and Lender have entered into that certain Loan and Security Agreement dated as of June 29, 2012, as amended by that certain Amendment No. 1 to Loan and Security Agreement dated as of July 24, 2012, as amended by that certain Amendment No. 2 to Loan and Security Agreement dated as of November 25, 2013, as amended by that certain Amendment No. 3 to the Loan and Security Agreement dated as of December 15, 2014, and as further amended by that certain Consent and Amendment No. 4 to the Loan and Security Agreement dated as of June 9, 2015 (as may be further amended, restated, supplemented or otherwise modified from time to time, the ***"Loan Agreement"),*** pursuant to which Lender has extended and make available to Borrowers certain extensions of credit.

B. Borrowers and Lender have agreed to amend the Loan Agreement upon the terms and conditions more fully set forth herein.

AGREEMENT

NOW, THEREFORE, in consideration of the foregoing Recitals and intending to be legally bound, the parties hereto agree as follows:

1. AMENDMENT.

1.1 Section 1.1 (Definitions and Rules of Construction). The following definitions set forth in Section 1.1 of the Loan Agreement shall be amended in their entirety and replaced with the following:

"Amortization Date" means October 1, 2016.

"Term Loan Maturity Date" means January 1, 2018.

2. BORROWERS' REPRESENTATIONS AND WARRANTIES. Each Borrower represents and warrants that:

(a) immediately upon giving effect to this Amendment (i) the representations and warranties contained in the Loan Documents are true, accurate and complete in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct as of such date), and (ii) no Event of Default has occurred and is continuing;

(b) such Borrower has the corporate or limited liability company, as applicable, power and authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

(c) the certificate of incorporation, bylaws and other organizational documents of such Borrower delivered to Lender on the Closing Date remain true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

(d) the execution and delivery by such Borrower of this Amendment and the performance by such Borrower of its obligations under the Loan Agreement, as amended by this Amendment, have been duly authorized by all necessary corporate or limited liability company, as applicable, action on the part of such Borrower;

(e) this Amendment has been duly executed and delivered by such Borrower and is the binding obligation of such Borrower, enforceable against it in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights; and

(f) as of the date hereof, such Borrower has no defenses against the obligations to pay any amounts under the Secured Obligations.

Each Borrower understands and acknowledges that Lender is entering into this Amendment in reliance upon, and in partial consideration for, the above representations and warranties, and agrees that such reliance is reasonable and appropriate.

3. LIMITATION. The amendments set forth in this Amendment shall be limited precisely as written and shall not be deemed (a) to be a waiver or modification of any other term or condition of the Loan Agreement or of any other instrument or agreement referred to therein or to prejudice any right or remedy which Lender may now have or may have in the future under or in connection with the Loan Agreement or any instrument or agreement referred to therein; or (b) to be a consent to any future amendment or modification or waiver to any instrument or agreement the execution and delivery of which is consented to hereby, or to any waiver of any of the provisions thereof. Except as expressly amended hereby, the Loan Agreement shall continue in full force and effect.

4. EFFECTIVENESS. This Amendment shall become effective upon the satisfaction of all the following conditions precedent:

4.1 Election to Extend; Fee. The Borrowers are electing to extend the Term Loan Maturity Date as set forth under the definition of "Term Loan Maturity Date" (as such term was defined in Amendment No. 3 to the Loan and Security Agreement dated as of December 15, 2014) and shall pay Agent a fully-earned, non-renewable facility fee equal to Two Hundred Fifty Thousand Dollars ($250,000.00) as required under the definition of "Financing Event".

4.2 Expenses. The Borrowers shall have paid all of Lender's reasonable, documented costs and out-of-pocket expenses in connection with this Amendment.

4.3 Amendment. The Lender shall have received duly executed counterparts of this Amendment signed by the parties hereto.

5. Future Amendments. To the extent Borrower and Lender enter into a substantial restructure of the Loan Agreement, in Lender's sole and absolute discretion and based upon its then current underwriting credit criteria, Lender agrees to apply the facility fee received pursuant to Section 4.1 hereof, towards the payment of any facility fee due in connection with such restructure.

6. COUNTERPARTS. This Amendment may be signed in any number of counterparts, and by different parties hereto in separate counterparts, with the same effect as if the signatures to each such counterpart were upon a single instrument. All counterparts shall be deemed an original of this Amendment.

7. INCORPORATION BY REFERENCE. The provisions of Section 11 of the Agreement shall be deemed incorporated herein by reference, *mutatis mutandis.*

[signature page follows]

IN WITNESS WHEREOF , the parties have duly authorized and caused this Amendment to be executed as of the date first written above.

BORROWERS :

INSMED INCORPORATED

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: CFO

INSMED PHARMACEUTICALS, INC.

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: CFO

TRANSAVE, LLC

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: CFO

CELTRIX PHARMACEUTICALS, Inc.

By: /s/ Andrew T. Drechsler
Name: Andrew T. Drechsler
Title: CFO

LENDER :

HERCULES CAPITAL FUNDING TRUST 2012-1

By: Hercules Technology Growth Capital, Inc., its servicer

By: /s/ Ben Bang
Name: Ben Bang
Its: Associate General Counsel

HERCULES CAPITAL FUNDING TRUST 2014-1

By: Hercules Technology Growth Capital, Inc., its servicer

By: /s/ Ben Bang
Name: Ben Bang
Its: Associate General Counsel

HERCULES TECHNOLOGY GROWTH CAPITAL, INC.

By: /s/ Ben Bang
Name: Ben Bang
Its: Associate General Counsel

[Signature page to Amendment No. 5 to Loan and Security Agreement]

Exhibit 10.14.1

CONFIDENTIAL TREATMENT HAS BEEN REQUESTED AS TO CERTAIN PORTIONS OF THIS DOCUMENT. EACH SUCH PORTION, WHICH HAS BEEN OMITTED HEREIN AND REPLACED WITH ASTERISKS (***), HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

AMENDMENT NO. 5
TO LICENSE AGREEMENT BETWEEN
INSMED INCORPORATED AND PARI PHARMA GMBH

This fifth amendment (" **Amendment No. 5** ") effective October 05 2015 (" **Amendment No. 5 Effective Date** ") to the License Agreement dated and effective the 25 th of April 2008 between PARI Pharma GmbH, a German corporation with a principal place of business at Moosstrasse 3, D-82319 Starnberg, Germany **("PARI** ") and Transave, Inc., a Delaware corporation, as amended by Amendment No. 1 the 24 th day of June 2009, Assignment and Amendment No. 2 the 22 nd day of December 2010, Amendment No. 3 the 6 th day of March 2012, and Amendment No. 4 the 21 st day of May 2012 (collectively, the " **Agreement** "), is entered into between PARI and Insmed Incorporated (successor in interest to Transave, Inc.), with registered offices at 10 Finderne Avenue, Building 10, Bridgewater, NJ 08807-3365 (" **Insmed** "). PARI and Insmed shall be referred to collectively as the " **Parties** ".

WHEREAS, the Parties now desire to amend the terms and conditions of the Agreement to reflect certain business discussions between the Parties, the current development status of the Drug Product and its use together with the Device in compassionate use, expanded access, named patient or similar programs (collectively "Early Access Programs").

NOW, THEREFORE, in consideration of the recitals set forth above, the mutual covenants, terms and conditions set forth below, and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties agree as follows:

1. Definitions. Capitalized terms used but not defined in this Amendment No. 5 shall have the meanings ascribed to them in the Agreement.

"Arikayce" means the same as Arikace.

"NTM" means Non-tuberculous Mycobacteria infections.

2. Section 4.2 (a). Section 4.2(a) shall be deleted and replaced as follows:

Subject to Section 4.2(b) below and the AKITA Rights, during the Term of this Agreement, PARI agrees that it and its Affiliates shall (x) not compete with Insmed in CF and/or Bronchiectasis with a Competing Nebulizer in the Transave Field, within the Transave Territory, (y) not engage in the research, development, manufacture and/or commercialization of amikacin for pulmonary administration using a Competing Nebulizer, and (z) not compete with Insmed in NTM with any *** (for clarity the *** shall not be considered a ***) for pulmonary administration of amikacin. In addition, during the term of this Agreement, PARI agrees that it and its Affiliates shall not compete with Insmed or otherwise engage in the research, development, manufacture and/or commercialization of any liposomal formulation of amikacin, tobramycin, ciprofloxacin, and levofloxacin for pulmonary administration, provided, however, that the foregoing restrictions in this sentence shall not apply with respect to (i) the right of any third party licensee (but only to the extent that

such right is existing and in effect as of the Effective Date) to research, develop, manufacture and/or commercialize any liposomal formulation of tobramycin, ciprofloxacin, and levofloxacin for pulmonary administration pursuant to any licensing agreements entered into by PARI or its Affiliates prior to the date of this Agreement, and (ii) the right of PARI and its Affiliates to enter into additional agreements that would be necessary or useful to exploit, but do not expand, existing rights under such licensing agreements referred to in (i), such as testing agreements, and clinical and commercial supply agreements, with any such third party licensee related to the research, development and manufacture and/or commercialization of products generated pursuant to those respective licensing agreements, except the foregoing restrictions in this sentence shall apply, notwithstanding (i) or (ii), with respect to any research, development, manufacture and/or commercialization of any such liposomal formulations for pulmonary administration using a Nebulizer that includes any developments or optimizations generated under Feasibility Statement of Work No. 3. Notwithstanding the foregoing, the Parties acknowledge and agree that PARI is able to supply medical device product information to customers and sell medical devices other than Competing Nebulizers to customers and patients indicated to deliver amikacin, tobramycin, ciprofloxacin, and levofloxacin (including liposomal formulations thereof) for any indication (including clinical development and clinical research), including CF and Bronchiectasis and NTM and that such uses shall not conflict with the prohibitions of this Section 4.2(a).

3. A new Section 7.2 (B) is hereby added:

First Right to Negotiate a License for * in *** .** Until *** PARI shall notify Insmed in writing in case it is approached by a third party or it would like to approach a third party for a license under PARI Intellectual Property regarding pulmonary delivery of *** to patients who suffer from *** via *** (the "*** Notice"). Within *** days after the date of the *** Notice Insmed shall inform PARI in writing if Insmed is interested to develop *** delivered via *** to patients suffering from *** and the Parties shall negotiate in good faith and execute an agreement which governs a license to deliver *** to patients suffering from *** (and potentially other indications) via *** (the "*** License Agreement"). Within *** after the date of the *** Notice the Parties shall negotiate in good faith and execute such *** License Agreement. If (i) Insmed informs PARI that it is not interested in a license to deliver *** via ***, (ii) Insmed does not inform PARI about its interest to enter into the *** License Agreement within *** after the date of the *** Notice, or (iii) the *** License Agreement is not executed within *** from the date of the *** Notice, then PARI shall be free to collaborate with any third party and to enter into a license agreement with any third party regarding the delivery of *** to patients suffering from ***.

4. **Section 7.1 (a).** The first sentence of Section 7.1(a) of the Agreement shall be deleted and replaced as follows:

(a) Insmed agrees to use Commercially Reasonable Efforts to pursue the clinical development of and to obtain Marketing Approval and reimbursement funding for CF for

the Drug Product intended for use with the Device in two (2) or more Major EU Countries, and after obtaining such Marketing Approval and reimbursement funding, to use Commercially Reasonable Efforts to market and sell the Drug Product with the Device in such Major EU Countries, except that Insmed may, in its sole discretion, permanently discontinue: development, seeking regulatory approval, or commercialization based on: safety issues, negative and/or unfavorable clinical trial results, lack of commercial viability, strength of competitors prohibiting an effective marketing of the Drug Product in the marketplace, or weak financial forecasts; provided, however, that in such event Insmed shall immediately notify PARI in writing of such decision and, if Insmed also fails to meet a milestone under Section 7.2A of the Agreement, then CF shall no longer be included in the Insmed Field and PARI's obligations under Section 4.2(a) shall no longer apply as to CF.

5. Section 7.2 (A). Section 7.2 (A) Insmed Development and Commercial Diligence for Non-tuberculous Mycobacteria Infections.

The table in Section 7.2A(a) shall be deleted and replaced with the following table:

Milestone Activity	Milestone Deadline
Completion of the INS-212 Clinical Study Report (CSR)	***
Completion of submission to US FDA for the Drug Product in NTM	***
First Commercial Sale of the Drug Product in US in NTM	***
First Commercial Sale of the Drug Product in the EU in NTM	***
First Commercial Sale of the Drug Product in Canada in NTM	***

The second paragraph of Section 7.2A(a) (directly below the table shown above) is hereby deleted.

In the third sentence of the third paragraph of Section 7.2A(a), "***" shall be replaced with "***".

In addition, the following sentences shall be added to the second paragraph of Section 7.2A(a):

"PARI's options to render the license granted hereunder non-exclusive, to terminate its obligations to not compete with Insmed or to terminate the license as described in this

*** Certain information on this page has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

Section shall only apply to (i) the US in case Insmed fails to meet the milestones for the US, (ii) Europe in case Insmed fails to meet the milestone for the EU; or (iii) the Territory in case both (i) and (ii) above occur.

If the diligence milestone First Commercial Sale of the Drug Product in the US in NTM is not met *** months after the applicable milestone deadline as set forth in the table above and First Commercial Sale of the Drug Product in the US did not occur or commercial sale has been ceased for another indication in the US, PARI shall be free to terminate the entire License with respect to US.

If the diligence milestone First Commercial Sale of the Drug Product in Canada in NTM is not met *** months after the applicable milestone deadline as set forth in the table above and First Commercial Sale of the Drug Product in Canada or the US did not occur or commercial sale has been ceased for another indication in Canada or the US or NTM in the US, PARI shall be free to terminate the entire License with respect to Canada.

If the diligence milestone First Commercial Sale of the Drug Product in the EU in NTM is not met *** months after the applicable milestone deadline as set forth in the table above and First Commercial Sale of the Drug Product did not occur or commercial sale has been ceased for another indication in the EU, PARI shall be free to terminate the entire License with respect to Europe.

In case the preconditions for the termination of the entire license in all regions, the US, Canada and Europe as set forth above, are given, PARI shall be free to terminate the entire license with respect to the Territory."

6. Section 8.8 (f). A new Section 8.8 (f) is hereby added to the Agreement:

"In addition to what is written in Section 8.8 (b) above, Insmed shall be permitted to use the Device for Early Access Programs and therefore may release the Devices supplied for clinical trial purposes also to individuals who will be participating in Early Access Programs and who have a need to access the Device in connection with use of the Device in such Early Access Programs, subject to the terms and conditions of this Agreement (including without limitation Section 7.7) and any Applicable Laws and Standards. Insmed shall be solely responsible for compliance with such Applicable Laws and Standards. The Parties anticipate that the same Device which is supplied for clinical trial purposes may be utilized in the Early Access Programs (with respect to both technical specifications and labelling). . If the Device does not meet such Applicable Laws and Standards for use in Early Access Programs, if requested by Insmed, PARI will use commercially reasonable efforts to ensure that the Device fulfills such Applicable Laws and Standards at Insmed's cost. Insmed shall be responsible for the traceability of the Devices and upon request by PARI Insmed shall within *** business days inform PARI whether a specific Device was used in an Early Access Program or in a clinical trial (including the unique identifier of the clinical trial) and in which country it was used. For clarity, to the extent that any of these programs reimburse Insmed, such reimbursement

shall not trigger the Royalty Term or the Annual Minimum Royalty as such programs are not commercial sales nor do these programs require Marketing Approval."

7. Section 11.5 (a). Section 11.5(a) of the Agreement is hereby amended by deleting the last sentence and replacing it with the following:

"Notwithstanding the foregoing, all press releases and similar disclosures issued by Insmed that contain material or substantive information regarding ARIKAYCE™ (liposomal amikacin for inhalation) as an inhaled product shall include the language set forth on Exhibit 11.5 attached hereto, as such Exhibit may be amended from time to time by PARI upon reasonable written notice to Insmed."

8. Amendment of Section 16.2. Section 16.2 of the Agreement is hereby amended by deleting the notice addresses for Insmed and replacing them with the following:

If to Insmed:
Insmed Incorporated
10 Finderne Avenue, Building 10
Bridgewater, NJ 08807
United States of America
Attn.: CEO
Fax: ***

with a copy to:
Insmed Incorporated
10 Finderne Avenue, Building 10
Bridgewater, NJ 08807
United States of America
Attn.: General Counsel
Fax: ***

9. Amendment of Exhibit 11.5. Exhibit 11.5 to the Agreement is hereby amended by deleting the first sentence and replacing it with the following:

"The Device shall be mentioned in every press release by Insmed that contains material or substantive information regarding ARIKAYCE™ (liposomal amikacin for inhalation), as an inhaled product."

10. Miscellaneous. Upon execution, this Amendment No. 5 shall be made part of the Agreement and shall be incorporated therein by reference. Except as provided herein, all other terms and conditions of the Agreement shall remain in full force and effect.

IN WITNESS WHEREOF, the Parties have executed this Amendment No. 5 as of the Amendment No. 5 Effective Date indicated above.

*** Certain information on this page has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

INSMED INCORPORATED		**PARI PHARMA GMBH**	
By:	/s/ William H. Lewis	By:	/s/ Dr. Martin Knoch
Name:	William H. Lewis	Name:	Dr. Martin Knoch
Title:	CEO & President	Title:	President
Date:	October 13, 2015	Date:	Oct. 13, 2015

Exhibit 10.14.2

CONFIDENTIAL TREATMENT HAS BEEN REQUESTED AS TO CERTAIN PORTIONS OF THIS DOCUMENT. EACH SUCH PORTION, WHICH HAS BEEN OMITTED HEREIN AND REPLACED WITH ASTERISKS (***), HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

AMENDMENT NO. 6
TO LICENSE AGREEMENT BETWEEN
INSMED INCORPORATED AND PARI PHARMA GMBH

This sixth amendment (" **Amendment No. 6** ") effective October 9, 2015 (" **Amendment No. 6 Effective Date** ") to the License Agreement dated and effective the 25 th of April 2008 between PARI Pharma GmbH, a German corporation with a principal place of business at Moosstrasse 3, D-82319 Starnberg, Germany (" **PARI** ") and Transave, Inc., a Delaware corporation, as amended by Amendment No. 1 the 24 th day of June 2009, Assignment and Amendment No. 2 the 22 nd day of December 2010, Amendment No. 3 the 6 th day of March 2012, Amendment No. 4 the 21 st day of May 2012, and Amendment No. 5 the 5th day of October 2015 (collectively, the " **Agreement** "), is entered into between PARI and Insmed Incorporated (successor in interest to Transave, Inc.), with registered offices at 10 Finderne Avenue, Building 10, Bridgewater, NJ 08807-3365 (" **Insmed** "). PARI and Insmed shall be referred to collectively as the " **Parties** ".

WHEREAS, the Parties now desire to amend the terms and conditions of the Agreement to reflect certain business discussion between the Parties and the current development status of the Drug Product.

NOW, THEREFORE, in consideration of the recitals set forth above, the mutual covenants, terms and conditions set forth below, and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties agree as follows:

1. **Definitions.** Capitalized terms used but not defined in this Amendment No. 6 shall have the meanings ascribed to them in the Agreement.

2. **Section 1.20A.** Section 1.20A is hereby added to the Agreement as follows:

1.20A " **Full Approval** " means receipt of a centralised marketing authorisation granted by the European Commission under Regulation (EC) 726/2004; and such a marketing authorization is not encumbered with specific conditions that form the basis of the requirement of annual renewal pursuant to Article 14(7) of Regulation (EC) 726/2004 and Regulation (EC) 507/2006.

3. **Section 1.48.** Section 1.48 is hereby deleted in its entirety and replaced with the following:

1.48 " **Royalty Term** " means on a country-by-country basis the period commencing on the date of First Commercial Sale of Drug Product, and ending upon the later of (a) Expiration of the (x) last Valid Claim covering the particular Device or (y) the Assigned Invention Patents, in each case, in the particular country in which such Product is sold, or (b) *** years after (X) First Commercial Sale of the Drug Product in such country outside of the European Union in the Insmed Territory or (Y) the date that all of the following criteria (i), (ii) and (iii) have occurred: (i) a Drug Product receives Full Approval, (ii) the First Commercial Sale of Drug Product in atleast *** Major

*** Certain information on this page has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

EU Countries and (iii) the First Commercial Sale in that particular country in the European Union.

4. **Section 6.3.** Section 6.3 of the Agreement is hereby amended by deleting "During the Royalty Term" and replacing it with "After the First Commercial Sale in the United States but no later than ***".

5. **Section 9.3.** Section 9.3 of the Agreement is hereby amended by adding "in the United States but no later than ***" after "First Commercial Sale" in both the first and second sentence of the section.

6. **Miscellaneous.** Upon execution, this Amendment No. 5 shall be made part of the Agreement and shall be incorporated therein by reference. Except as provided herein, all other terms and conditions of the Agreement shall remain in full force and effect.

*** Certain information on this page has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the Parties have executed this Amendment No. 6 as of the Amendment No. 6 Effective Date indicated above.

INSMED INCORPORATED		**PARI PHARMA GMBH**	
By:	/s/ William H. Lewis	By:	/s/ Dr. Martin Knoch
Name:	William H. Lewis	Name:	Dr. Martin Knoch
Title:	CEO & President	Title:	President
Date:	Oct. 13, 2015	Date:	Oct. 13, 2015

Exhibit 10.17.1

FIRST AMENDMENT TO LEASE

THIS FIRST AMENDMENT TO LEASE (the " **Amendment** ") is entered into this 29 day of April , 2014, between DENVER ROAD, LLC, a New Jersey limited liability company (" **Landlord** "), and INSMED INCORPORATED, a Virginia corporation (" **Tenant** "). For purposes of this Amendment, the " **Effective Date** " shall be the date this Amendment has been executed and delivered by Landlord and Tenant.

Landlord and Tenant are parties to a certain Lease (the " **Lease** ") dated December 31, 2013, covering premises deemed to contain approximately 27,435 rentable square feet (the " **Existing Premises** ") located in Building 10 (the " **Building** "), 10 Finderne Avenue, Bridgewater, New Jersey, as more particularly described in the Lease.

By written notice dated February 19, 2014, Tenant notified Landlord, pursuant to Section 15.2 of the Lease, that (i) Tenant desires to lease a portion of the Available Third Floor Space (as defined in said Section 15.2), and (ii) Tenant desires to lease a portion of the First Floor Space (as defined in said Section 15.2). The portion of the Available Third Floor Space to be leased by Tenant consists of an area deemed to contain 14,121 rentable square feet located on the third (3rd) floor of the Building, as shown on the plan attached hereto and made a part hereof as Exhibit A (the " **Third Floor Area** "), and the portion of the First Floor Space to be leased by Tenant consists of an area deemed to contain 1,301 rentable square feet located on the first (1st) floor of the Building, as shown on the plan attached hereto and made a part hereof as Exhibit B (the " **First Floor Area** ") (the Third Floor Area and the First Floor Area are sometimes referred to together herein as the " **New Space** ", and together are deemed to contain 15,422 rentable square feet). The purpose of this Amendment is to document the leasing of the New Space, as provided in said Section 15.2, and otherwise subject to and in accordance with the terms and conditions set forth in this Amendment.

For good and valuable consideration the receipt and sufficiency of which is acknowledged by Landlord and Tenant, and intending to be legally bound hereby, Landlord and Tenant agree as follows:

1. Effective as of the Effective Date, (i) Landlord shall deliver possession of the New Space to Tenant, and the Premises shall for all purposes under the Lease, as amended by this Amendment, include both the Existing Premises and the New Space, and (ii) the total space being leased by Landlord to Tenant, and by Tenant from Landlord, under the Lease, as amended by this Amendment (and, therefore, the " **Premises** ", as defined in the Lease) shall be deemed to contain a total of 42,857 rentable square feet.

2. The Term of the Lease with respect to the New Space shall commence upon the Effective Date, and shall end coterminously with the Term for the Existing Premises, on the Expiration Date (as defined in the Lease).

3. With respect to the New Space, the following terms and conditions shall be applicable:

(a) Upon execution of this Amendment by Landlord and Tenant, Landlord shall deliver possession of the New Space to Tenant, and Tenant shall accept possession of the

New Space, vacant and in its current "AS IS" condition. Landlord's obligations under clause (i) of the second sentence of Section 1.4 of the Lease shall not be applicable to the New Space.

(b) Commencing as of the seven (7) month anniversary of the Effective Date (the " **New Space Rent Commencement Date** "), and continuing throughout the remainder of the Term, Tenant shall pay to Landlord Fixed Rent (as defined in the Lease) for the New Space at the following rates for the following periods (in addition to the Fixed Rent payable by Tenant for the Existing Premises under the Lease, which shall remain unaffected by this Amendment):

(i) $246,752.04 (i.e., $16.00 per rentable square foot of the New Space), per annum, payable in equal monthly installments of $20,562.67, for the period from the New Space Rent Commencement Date, to and including May 31, 2015;

(ii) $254,463.00 (i.e., $16.50 per rentable square foot of the New Space), per annum, payable in equal monthly installments of $21,205.25, for the period from June 1, 2015, to and including May 31, 2016;

(iii) $262,173.96 (i.e., $17.00 per rentable square foot of the New Space), per annum, payable in equal monthly installments of $21,847.83, for the period from June 1, 2016, to and including May 31, 2017;

(iv) $269,885.04 (i.e., $17.50 per rentable square foot of the New Space), per annum, payable in equal monthly installments of $22,490.42, for the period from June 1, 2017, to and including May 31, 2018;

(v) $277,596.00 (i.e., $18.00 per rentable square foot of the New Space), per annum, payable in equal monthly installments of $23,133.00, for the period from June 1, 2018, to and including May 31, 2019; and

(vi) $285,306.96 (i.e., $18.50 per rentable square foot of the New Space), per annum, payable in equal monthly installments of $23,775.58, for the period from June 1, 2019, to and including November 30, 2019.

Provided no Event of Default (as defined in the Lease) is then in existence, Tenant shall receive a credit against the Fixed Rent first payable under this Amendment for the New Space in the amount of $112,161.12, to be applied until exhausted against the monthly installments of Fixed Rent for the New Space first coming due from and after the New Space Rent Commencement Date. In addition, Tenant shall not be required to pay any Tax Payment (as defined in the Lease) or Operating Payment (as defined in the Lease) with respect to the New Space allocable to any period prior to the date such credit against Fixed Rent is exhausted.

(c) The provisions of Section 1.5 of the Lease shall be applicable to Tenant's lease of the New Space pursuant to this Amendment, except as follows:

(i) As to the portion of the Available Third Floor Space being leased by Tenant hereunder (i.e., the Third Floor Area), Landlord and Tenant acknowledge that the location and configuration of the Third Floor Area reflects a modification of the configuration of the existing common corridor abutting said area from that shown on Exhibit G-l attached to the Lease (in that the wall between the Third Floor Area and such corridor shall be straight, as

shown on Exhibit A attached hereto, rather than a series of angled abutments, as shown on Exhibit G-l attached to the Lease). Tenant acknowledges and confirms that all modifications to the existing corridor required to so modify the wall between the Third Floor Area and said corridor shall be performed by Tenant as part of the Initial Tenant Work (as defined in the Lease) with respect to the Third Floor Area. Landlord agrees that Tenant shall not be required to restore said corridor at the expiration of the Lease to its condition prior to the modification of the configuration thereof as described above.

(ii) The Tenant Allowance (as defined in the Lease) with respect to the Initial Tenant Work for the Third Floor Area shall equal $231,073.22.

(iii) The Tenant Allowance with respect to the Initial Tenant Work for the First Floor Area shall equal $21,289.30.

(iv) Tenant acknowledges that the First Floor Area is not separately demised, and that it shall be Tenant's responsibility, as part of the Initial Tenant Work for the First Floor Area, to construct walls, doorways and other improvements required to fully enclose and separately demise the First Floor Area (the " **Demising Work** "); provided, however, that the Initial Tenant Work (and, if applicable, the Demising Work) for the First Floor Area shall preserve the doorway to the mechanical room area shown on Exhibit B attached hereto, and at all times during the Term of the Lease, Landlord shall be entitled to access such mechanical room through the First Floor Area and such doorway.

(d) Notwithstanding anything to the contrary contained in the Lease or this Amendment, unless and to the extent that Landlord provides notice to Tenant to the contrary (Landlord will not provide such notice later than nine (9) months prior to the Expiration Date and any later notice shall be deemed null and void) prior to the expiration or sooner termination of the Lease, Tenant shall remove, prior to the expiration of the Lease (or within thirty (30) days following the earlier termination thereof), Tenant Improvements (as defined in the Lease) that consist of Alterations constructed as part of the Initial Tenant Work (as defined in the Lease) or to the Third Floor Area or the First Floor Area under this Amendment that (i) are to portions of the Premises that are to consist of laboratory space or are to be used for laboratory purposes, (ii) constitute Tenant's Rooftop Equipment (as defined in the Lease), or (iii) constitute an internal staircase connecting the Existing Premises to the Third Floor Area or the First Floor Area.

4. With respect to all periods from and after the Effective Date, (i) Tenant's Share (as defined in the Lease) for the Premises (i.e., the Existing Premises and the New Space) shall be 10.2087%, and (ii) Tenant's Building 10 Share (as defined in the Lease) for the Premises (i.e., the Existing Premises and the New Space) shall be 66.2887%.

5. Landlord shall not be required to provide interior cleaning services to the laboratory areas located in the Third Floor Area (the " **Third Floor Laboratory Area** ") and to the First Floor Area under Section 4.6 of the Lease. Landlord shall provide Tenant with a credit against the Fixed Rent payable by Tenant for the New Space under this Amendment in an annual amount equal to the product of (i) the per rentable square foot amount paid by Landlord per annum for standard office cleaning services at the Complex (as defined in the Lease) times (ii) the number of rentable square feet of the Third Floor Laboratory Area and the First Floor Area. Landlord shall notify Tenant from time to time of Landlord's calculation of such credit and any change thereto. Tenant shall be solely responsible, at Tenant's sole cost and expense, for

providing cleaning services for the Third Floor Laboratory Area and the First Floor Area, and shall keep and maintain the Third Floor Laboratory Area and the First Floor Area (including all bathroom and shower facilities therein) at all times in a clean, sanitary and safe condition. Tenant shall indemnify, defend and hold harmless Landlord from and against all liability arising in connection with all activities of Tenant and any Tenant Party in the Third Floor Laboratory Area and the First Floor Area, including but not limited to liability arising from injuries (including death) resulting from or in connection with such activities unless due to Landlord's gross negligence or willful misconduct.

6. Subject to the terms hereof, Tenant shall be provided exclusive use of the first (1st) floor point of entry room (" **POE Room** "), for the uses for which the Premises may be used, in the location identified on Exhibit B attached hereto. Except for the payment of Fixed Rent, charges for Building-standard electricity, Tax Payments (as defined in the Lease) and Operating Payments (as defined in the Lease), Tenant's obligations under the Lease with respect to the Premises shall be applicable to Tenant's use and occupancy of the POE Room. Landlord shall not be required to provide any services to the POE Room, or any allowance for the construction of Alterations in the POE Room. Tenant shall accept the POE Room in its "AS IS" condition, as of Landlord's delivery of possession thereof to Tenant (the POE Room to be so delivered at the same time as Landlord delivers possession of the First Floor Area). In the event Landlord requires the use of the POE Room by any entity other than Tenant, Landlord shall provide prior written notice to Tenant along with plans as to how Landlord will demise the POE Room for use by another Tenant. Prior to any other tenant's use of the POE Room, Landlord shall demise the POE Room into a separate space with a separate entry at Landlord's sole cost and expense. Prior to performing any work, Landlord shall submit its demising plan to Tenant for Tenant's prior written approval, which approval shall not be unreasonably withheld, conditioned or delayed, but which approval shall take into consideration Tenant's required security level. Demising costs shall include, without limitation, installation of any additional entrances, the relocation of equipment including but not limited to transformers and electrical panels and relocation or removal of any obstructions blocking or interfering with any new entrance.

7. Each party covenants, warrants and represents to the other party that no broker, other than Jones Lang LaSalle and Linque Management Company, Inc. (together, " **Broker** "), was instrumental in bringing about or consummating this Amendment and that it has had no conversations or negotiations with any broker except Broker concerning the leasing of the New Space. Each party agrees to indemnify and hold harmless the other party against and from any claims for any brokerage commissions and all costs, expenses and liabilities in connection therewith, including, without limitation, reasonable attorneys' fees and expenses, arising out of any conversations or negotiations had by such party with any broker other than Broker. Landlord agrees to pay Broker any commission owing to Broker in connection with this Amendment pursuant to a separate agreement or agreements.

8. If there is any conflict between the terms and provisions of the Lease and the terms and provisions of this Amendment, the terms and provisions of this Amendment shall prevail. Landlord and Tenant ratify and affirm the Lease as modified by this Amendment. Except as modified by this Amendment, the Lease shall remain unmodified, in full force and effect. Except as herein otherwise expressly provided, or except as the terms of the Lease may be in conflict with or inconsistent with the terms of this Amendment, all of the terms, covenants and provisions of the Lease are hereby incorporated into and made a part of this Amendment as if fully set forth herein.

9. This Amendment may be executed and delivered by the undersigned in counterparts. The electronically transmitted signature of a party to this Amendment shall be binding upon such party.

IN WITNESS WHEREOF, Landlord and Tenant have executed this Amendment as of the day and year first above written.

LANDLORD:

DENVER ROAD, LLC

By /s/ Menashe Frankel
Name: Menashe Frankel
Title: Member

TENANT:

INSMED INCORPORATED

By /s/ William H. Lewis
Name: William H. Lewis
Title: President and CEO

EXHIBIT A

The Third Floor Area

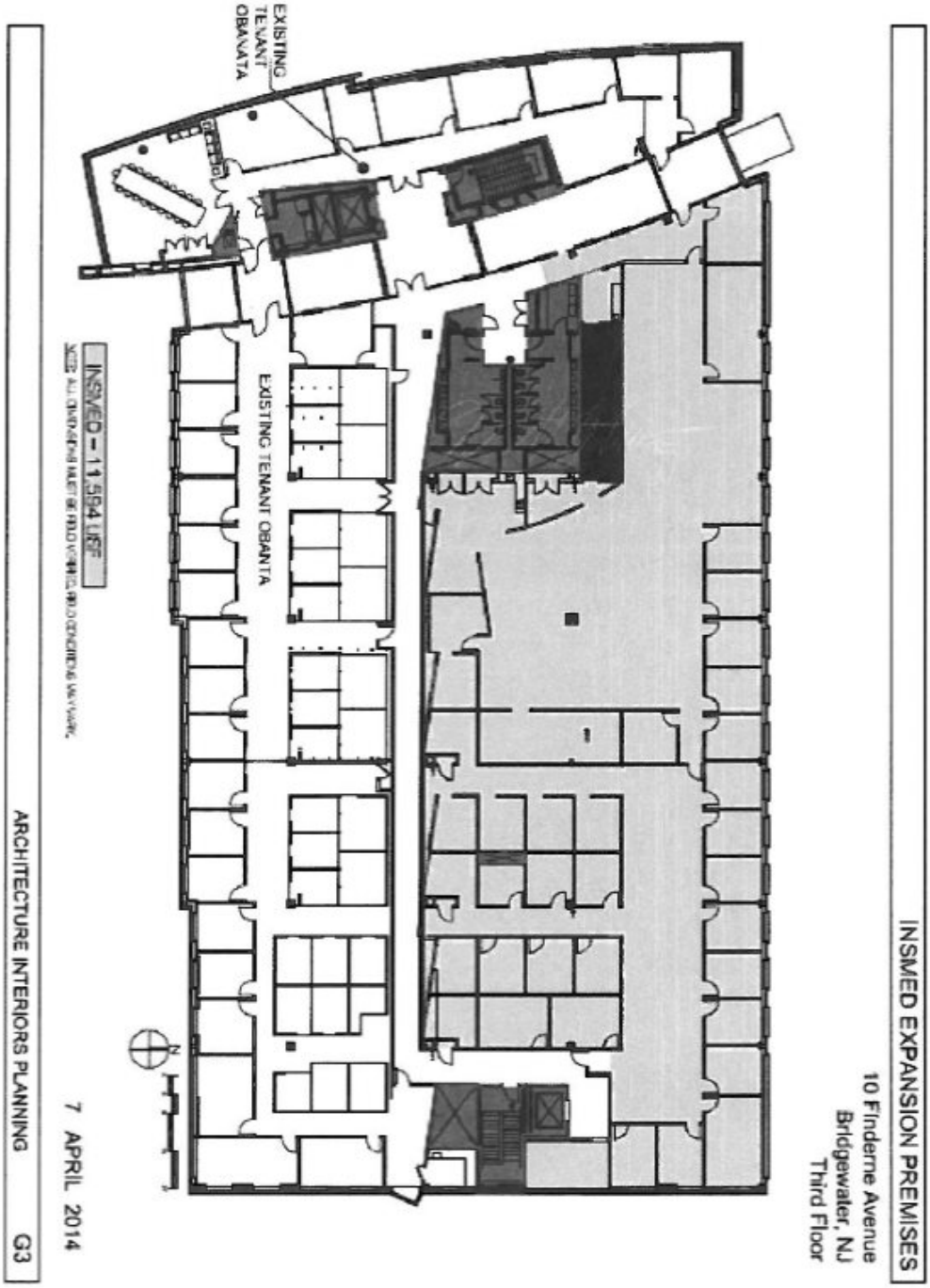


EXHIBIT B

The First Floor Area

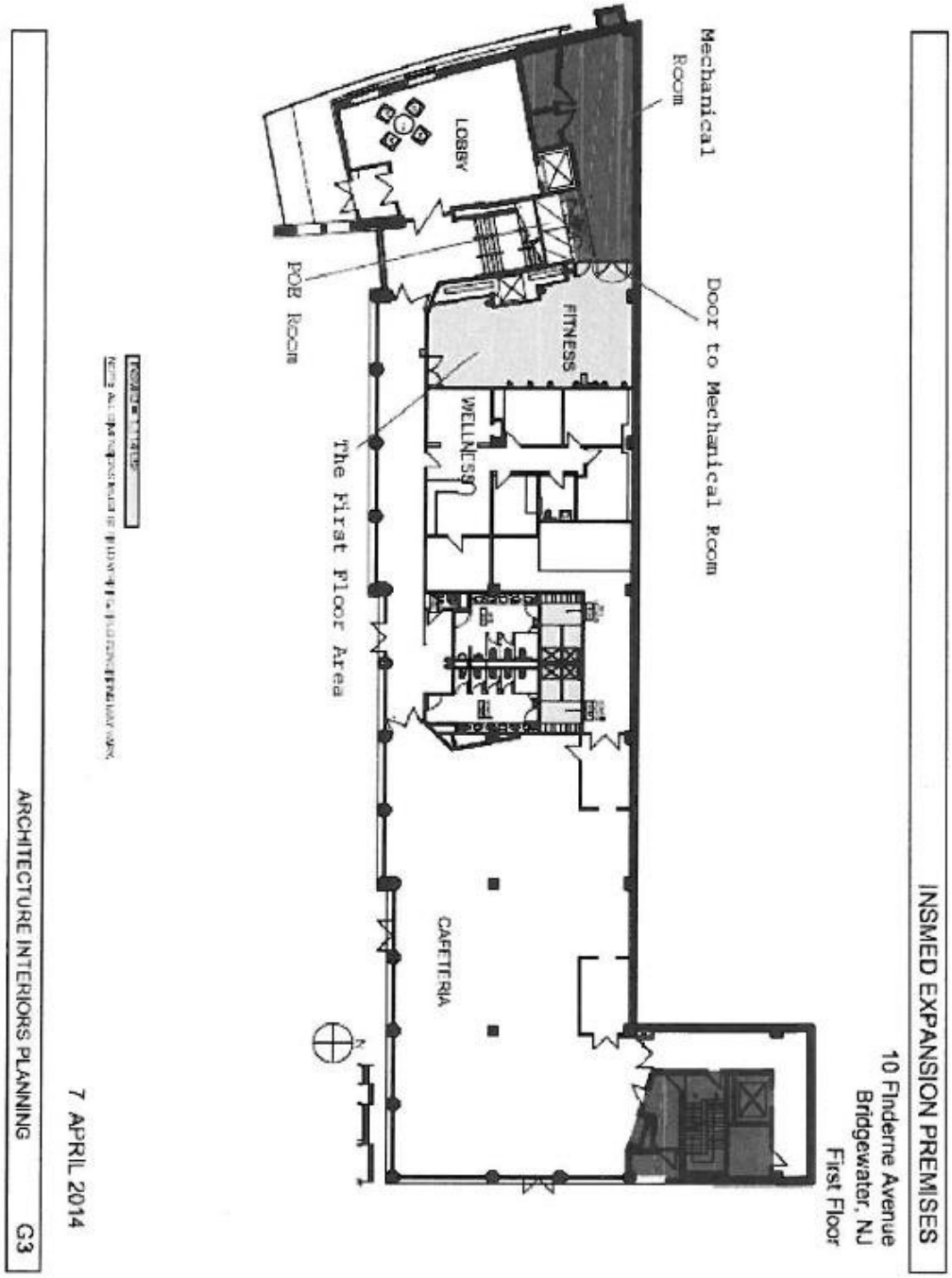


Exhibit 10.17.2

SECOND AMENDMENT TO LEASE

THIS SECOND AMENDMENT TO LEASE (the " **Amendment** ") is entered into this 20th day of November, 2015, between DENVER ROAD, LLC, a New Jersey limited liability company (" **Landlord** "), and INSMED INCORPORATED, a Virginia corporation (" **Tenant** "). For purposes of this Amendment, the " **Effective Date** " shall be the date this Amendment has been executed and delivered by Landlord and Tenant.

Landlord and Tenant are parties to a certain Lease (the " **Original Lease** ") dated December 31, 2013, as amended by a certain First Amendment to Lease (the " **First Amendment** ") dated April 29, 2014 (the Original Lease and the First Amendment are referred to together herein as the " **Lease** "). The Lease covers premises deemed to contain approximately 42,857 rentable square feet (the " **Existing Premises** ") located in Building 10 (the " **Building** "), 10 Finderne Avenue, Bridgewater, New Jersey, as more particularly described in the Lease.

Landlord and Tenant desire for Tenant to lease additional premises consisting of an area deemed to contain 13,760 rentable square feet located on the third (3rd) floor of the Building, as shown on the plan attached hereto and made a part hereof as Exhibit A (the " **2015 New Space** "), and to otherwise amend certain terms and provisions of the Lease, subject to and in accordance with the terms and conditions set forth in this Amendment.

For good and valuable consideration the receipt and sufficiency of which is acknowledged by Landlord and Tenant, and intending to be legally bound hereby, Landlord and Tenant agree as follows:

1. Effective as of the Effective Date, (i) Landlord shall deliver possession of the 2015 New Space to Tenant, and the Premises shall for all purposes under the Lease, as amended by this Amendment, include both the Existing Premises and the 2015 New Space, and (ii) the total space being leased by Landlord to Tenant, and by Tenant from Landlord, under the Lease, as amended by this Amendment (and, therefore, the " **Premises** ", as defined in the Lease) shall be deemed to contain a total of 56,617 rentable square feet.

2. The Term of the Lease with respect to the 2015 New Space shall commence upon the Effective Date, and shall end coterminously with the Term for the Existing Premises, on the Expiration Date (as defined in the Lease).

3. With respect to the 2015 New Space, the following terms and conditions shall be applicable:

(a) Upon execution of this Amendment by Landlord and Tenant, Landlord shall deliver possession of the 2015 New Space to Tenant, and, subject to Tenant completing the 2015 New Space Landlord Work (as hereinafter defined), Tenant shall accept possession of the 2015 New Space, vacant and in its current "AS IS" condition. Landlord's obligations under clause (i) of the second sentence of Section 1.4 of the Lease shall not be applicable to the 2015 New Space. Landlord shall perform the following work in and to the 2015 New Space (the " **2015 New Space Landlord Work** ") at Landlord's cost: (i) repair or replace any broken or malfunctioning window blinds or treatments in the 2015 New Space, and (ii) by December 31, 2015, replace contactors, motors and filters in the twenty-six (26) VAV boxes in the 2015 New Space identified on Exhibit D attached hereto and made a part hereof, such that said VAV boxes

shall be in proper working condition, and remove the existing crossover duct and cap the tap thereof in the 2015 New Space (said work described in this clause (ii) being referred to as the " **VAV Box Work** "). Tenant shall be entitled to confirm that the VAV Box Work has been completed.

(b) Commencing as of the date that is one hundred twenty (120) days after the Effective Date (the " **2015 New Space Rent Commencement Date** "), and continuing throughout the remainder of the Term, Tenant shall pay to Landlord Fixed Rent (as defined in the Lease) for the 2015 New Space at the following rates for the following periods (in addition to the Fixed Rent payable by Tenant for the Existing Premises under the Lease, which shall remain unaffected by this Amendment):

(i) $247,680.00 (i.e., $18.00 per rentable square foot of the 2015 New Space), per annum, payable in equal monthly installments of $20,640.00, for the period from the 2015 New Space Rent Commencement Date to and including the day immediately preceding the one (1) year anniversary of the 2015 New Space Rent Commencement Date;

(ii) $254,559.96 (i.e., $18.50 per rentable square foot of the 2015 New Space), per annum, payable in equal monthly installments of $21,213.33, for the period from the one (1) year anniversary of the 2015 New Space Rent Commencement Date to and including the day immediately preceding the two (2) year anniversary of the 2015 New Space Rent Commencement Date;

(iii) $261,440.04 (i.e., $19.00 per rentable square foot of the 2015 New Space), per annum, payable in equal monthly installments of $21,786.67, for the period from the two (2) year anniversary of the 2015 New Space Rent Commencement Date to and including the day immediately preceding the three (3) year anniversary of the 2015 New Space Rent Commencement Date; and

(iv) $268,320.00 (i.e., $19.50 per rentable square foot of the 2015 New Space), per annum, payable in equal monthly installments of $22,360.00, for the period from the three (3) year anniversary of the 2015 New Space Rent Commencement Date to and including November 30, 2019.

Provided no Event of Default (as defined in the Lease) is then in existence, Tenant shall receive a credit against the Fixed Rent first payable under this Amendment for the 2015 New Space in the amount of $66,420.00, to be applied until exhausted against the monthly installments of Fixed Rent for the 2015 New Space first coming due from and after the 2015 New Space Rent Commencement Date.

(c) The provisions of Section 1.5 of the Original Lease shall be applicable to Tenant's lease of the 2015 New Space pursuant to this Amendment, except that the Tenant Allowance (as defined in the Original Lease) with respect to the Initial Tenant Work for the 2015 New Space shall equal $165,120.00.

(d) Notwithstanding anything to the contrary contained in the Lease or this Amendment, unless and to the extent that Landlord provides notice to Tenant to the contrary (Landlord will not provide such notice later than nine (9) months prior to the Expiration Date and any later notice shall be deemed null and void) prior to the expiration or sooner termination of

the Lease, Tenant shall remove, prior to the expiration of the Lease (or within thirty (30) days following the earlier termination thereof), Tenant Improvements (as defined in the Original Lease) that consist of Alterations (as defined in the Original Lease) constructed as part of the Initial Tenant Work (as defined in the Original Lease) or to the Third Floor Area or the First Floor Area (as such terms are defined in the First Amendment) or to the 2015 New Space under this Amendment that (i) are to portions of the Premises that are to consist of laboratory space or are to be used for laboratory purposes, (ii) constitute Tenant's Rooftop Equipment (as defined in the Original Lease), or (iii) constitute an internal staircase connecting portions of the Premises.

4. With respect to the 2015 New Space only, (i) the Base Tax Year (as defined in the Original Lease) and the Base Operating Year (as defined in the Original Lease) shall mean the calendar year 2016, (ii) Tenant's Share (as defined in the Original Lease) for the 2015 New Space shall be 3.2777%, and (ii) Tenant's Building 10 Share (as defined in the Original Lease Lease) for the 2015 New Space shall be 21.2382%. Tenant's obligations to pay Tax Payments (as defined in the Original Lease) and Operating Payments (as defined in the Original Lease) with respect to the Existing Premises shall remain unaffected by this Amendment.

5. Any laboratory areas located in the 2015 New Space shall be included in and constitute a part of Third Floor Laboratory Area (as defined in the First Amendment) for purposes of Section 5 of the First Amendment.

6. The number of Tenant's Reserved Spaces (as defined in the Original Lease), to be governed by Section 3.4.2 of the Original Lease is hereby increased from ten (10) to twenty (20) reserved parking spaces, and shall included, in addition to the parking spaces shown on Exhibit J attached to the Original Lease, the parking spaces identified on the plan attached hereto and made a part hereof as Exhibit B .

7. The provisions of Section 4.2 of the Original Lease shall be applicable to the 2015 New Space for the purpose of determining Tenant's cost for electricity furnished to the 2015 New Space.

8. (a) The amount of the Security Deposit (as defined in the Original Lease) under Section 11.6 of the Original Lease shall be $200,000. Tenant shall cause a replacement letter of credit (or amendment to the existing letter of credit held by Landlord under said Section 11.6) to be issued to Landlord in such amount (and in the event of a replacement letter of credit, upon receipt thereof Landlord shall return the replaced letter of credit to Tenant).

(b) Section 11.6(e) of the Original Lease is deleted in its entirety.

9. Each party covenants, warrants and represents to the other party that no broker, other than Jones Lang LaSalle and Linque Management Company, Inc. (together, " **Broker** "), was instrumental in bringing about or consummating this Amendment and that it has had no conversations or negotiations with any broker except Broker concerning the leasing of the 2015 New Space. Each party agrees to indemnify and hold harmless the other party against and from any claims for any brokerage commissions and all costs, expenses and liabilities in connection therewith, including, without limitation, reasonable attorneys' fees and expenses, arising out of any conversations or negotiations had by such party with any broker other than Broker. Landlord agrees to pay Broker any commission owing to Broker in connection with this Amendment pursuant to a separate agreement or agreements, and agrees to indemnify and hold

harmless Tenant from and against any claims by Broker for any commissions owing with respect to Tenant's leasing of the 2015 New Space.

10. If there is any conflict between the terms and provisions of the Lease and the terms and provisions of this Amendment, the terms and provisions of this Amendment shall prevail. Landlord and Tenant ratify and affirm the Lease as modified by this Amendment. Except as modified by this Amendment, the Lease shall remain unmodified, in full force and effect. Except as herein otherwise expressly provided, or except as the terms of the Lease may be in conflict with or inconsistent with the terms of this Amendment, all of the terms, covenants and provisions of the Lease are hereby incorporated into and made a part of this Amendment as if fully set forth herein.

11. This Amendment may be executed and delivered by the undersigned in counterparts. The electronically transmitted signature of a party to this Amendment shall be binding upon such party.

12. Tenant shall have the exclusive right to utilize the first floor lobby of the Building, as shown on the plan attached hereto and made a part hereof as Exhibit C , as a reception area at no additional rental charge; provided that ingress and egress to and from the remainder of the Building is in compliance with applicable codes requirements. Such area shall constitute a portion of the Premises, and Tenant's obligations under the Lease, as amended by this Amendment, as to the Premises shall be applicable to said area. Tenant shall reasonably cooperate with Landlord to coordinate security and code compliant ingress and egress to and from the remainder of the Building.

IN WITNESS WHEREOF, Landlord and Tenant have executed this Amendment as of the day and year first above written.

LANDLORD:

DENVER ROAD, LLC

By /s/ Menashe Frankel
Name: Menashe Frankel
Title: Managing Member

TENANT:

INSMED INCORPORATED

DocuSigned by:

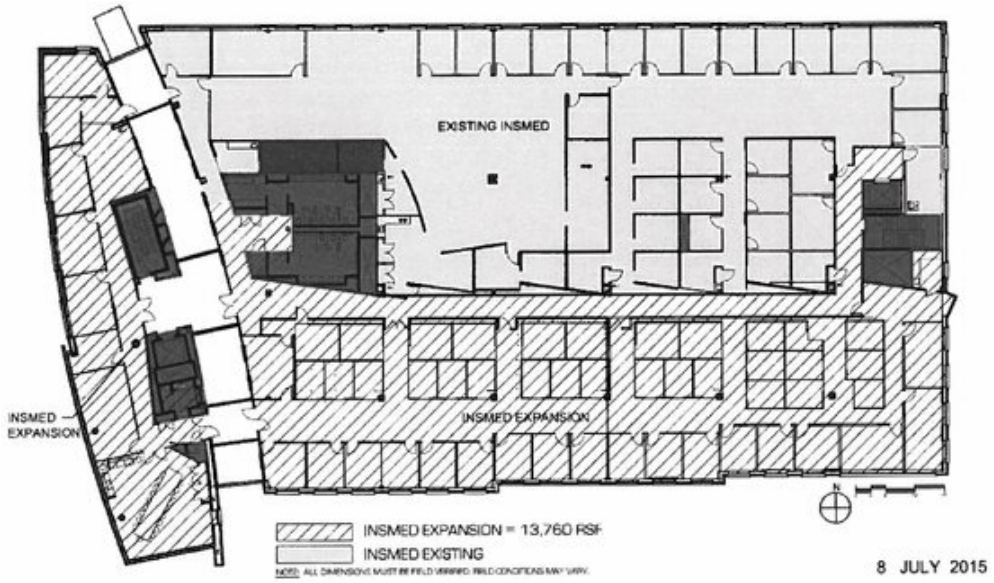
By /s/ Will Lewis
Name: Will Lewis
Title: Chief Executive Officer

EXHIBIT A

The 2015 New Space

INSMED EXPANSION PREMISES

10 Finderne Avenue Bridgewater, NJ Third Floor



ARCHITECTURE INTERIORS PLANNING G3

EXHIBIT B

Tenant's Additional Reserved Parking

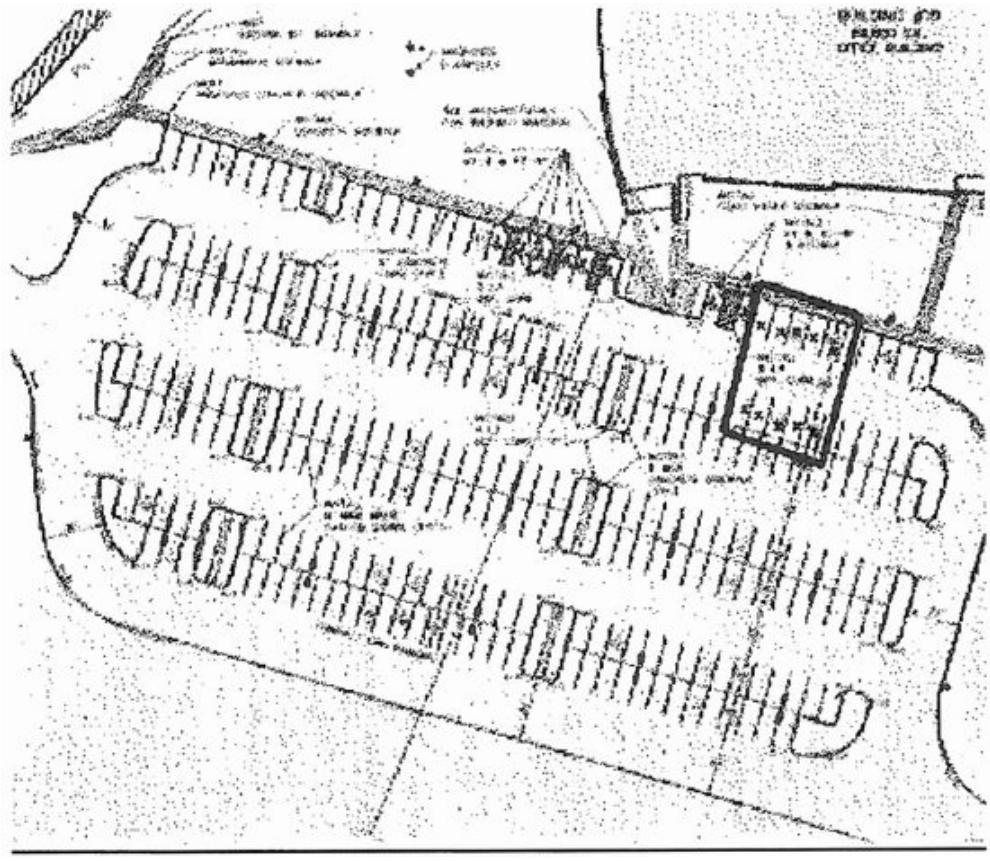


EXHIBIT C

First Floor Lobby

10 Finderne Avenue
Bridgewater, NJ
First Floor

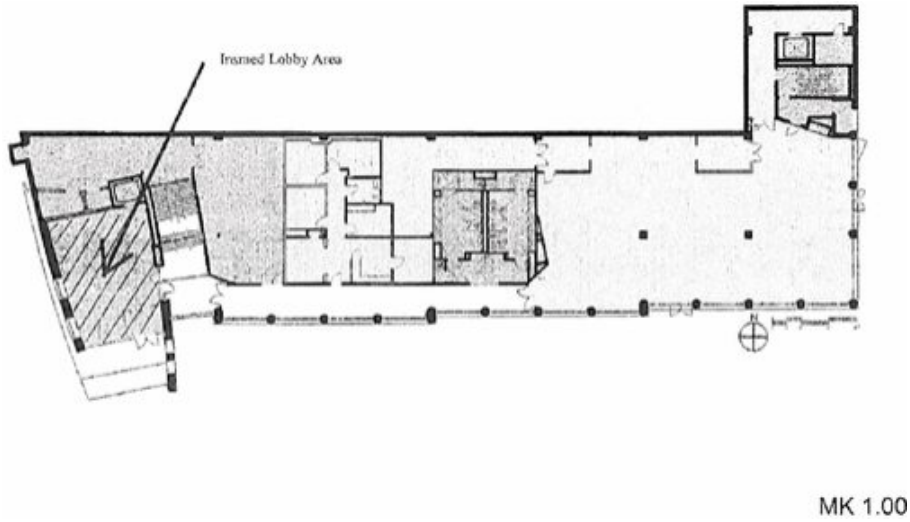
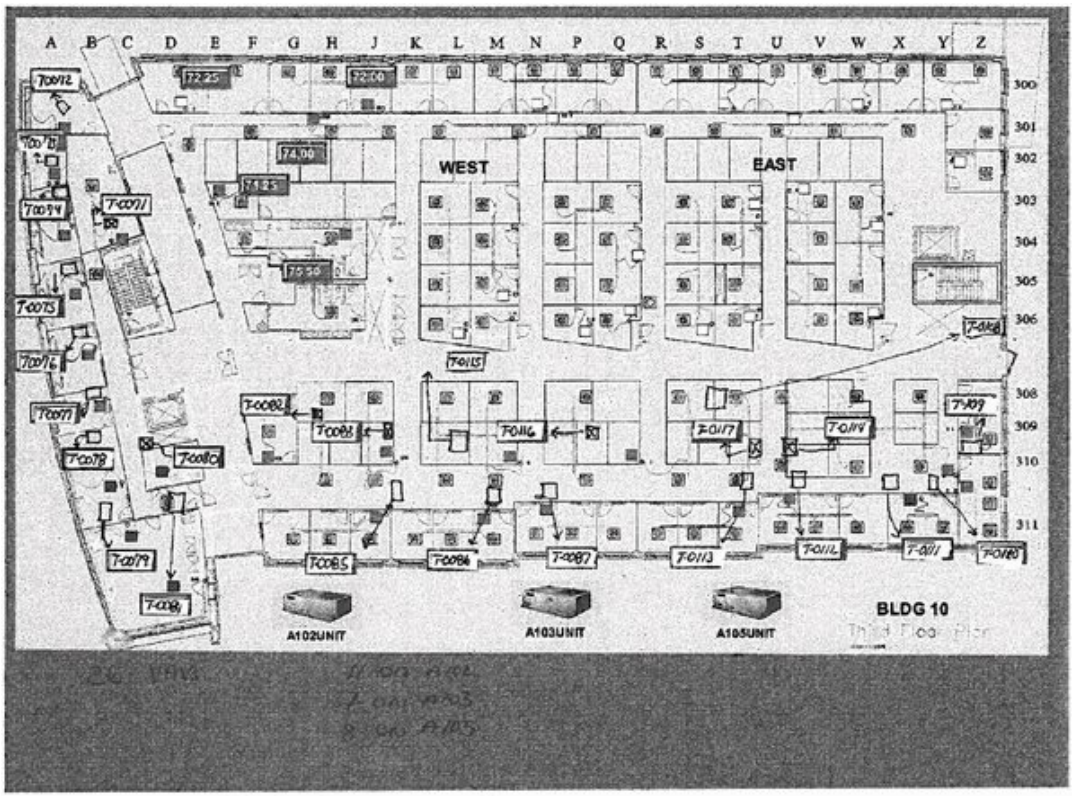


EXHIBIT D

VAV Boxes

BLDG. 10 3RD FLR 11/4/2015 10:54:04 AM



QuickLinks -- Click here to rapidly navigate through this document

EXHIBIT 21.1

APPENDIX A
LIST OF SUBSIDIARIES

Name	Jurisdiction of Incorporation
Insmed Pharmaceuticals, Inc.	Virginia
Celtrix Pharmaceuticals, Inc.	Delaware
Insmed Limited	England and Wales
Transave, LLC	Delaware
Insmed Holdings Limited	Ireland
Insmed Ireland Limited	Ireland
Insmed Germany GmbH	Germany
Insmed France SAS	France
Insmed Netherlands B.V.	Netherlands

QuickLinks

QuickLinks -- Click here to rapidly navigate through this document

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement on Form S-3 Nos. 333-188851 and 333-196418 of Insmed Incorporated, and

(2) Registration Statements on Form S-8 Nos. 333-39200, 333-87878, 333-129479, 333-175532, 333-188852 and 333-204503 of Insmed Incorporated;

of our reports dated February 25, 2016, with respect to the consolidated financial statements of Insmed Incorporated and the effectiveness of internal control over financial reporting of Insmed Incorporated included in this Annual Report (Form 10-K) of Insmed Incorporated for the year ended December 31, 2015.

/s/ Ernst & Young LLP

Iselin, New Jersey
February 25, 2016

QuickLinks

EXHIBIT 31.1

Section 302 Certification

I, William H. Lewis, Chief Executive Officer of Insmed Incorporated, certify that:

(1) I have reviewed this annual report on Form 10-K of Insmed Incorporated;

(2) Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

(3) Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

(4) The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

(5) The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 25, 2016

By: /s/ William H. Lewis

William H. Lewis
Chief Executive Officer (Principal Executive Officer) and Director

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EXHIBIT 31.2

CERTIFICATION PURSUANT TO

18 USC. SECTION 1350,

AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2003

In connection with this Annual Report on Form 10-K of Insmed Incorporated (the "Company") for the period ended December 31, 2015 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, William H. Lewis, Chief Executive Officer of the Company, certify, pursuant to 18 USC. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2003, that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

By: /s/ William H. Lewis

William H. Lewis
Chief Executive Officer
(Principal Executive Officer)
and Director

February 25, 2016

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Insmed Incorporated 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 Form 10-K), irrespective of any general incorporation language contained in such filing.

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EXHIBIT 32.1

Section 302 Certification

I, Andrew T. Drechsler, Chief Financial Officer of Insmed Incorporated, certify that:

(1) I have reviewed this annual report on Form 10-K of Insmed Incorporated;

(2) Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

(3) Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

(4) The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

(5) The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 25, 2016

/s/ Andrew T. Drechsler

Andrew T. Drechsler
Chief Financial Officer
(Principal Financial and Accounting Officer)

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EXHIBIT 32.2

CERTIFICATION PURSUANT TO

18 USC. SECTION 1350,

AS ADOPTED PURSUANT TO

SECTION 906 OF THE SARBANES-OXLEY ACT OF 2003

In connection with this Annual Report on Form 10-K of Insmed Incorporated (the "Company") for the period ended December 31, 2015 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Andrew T. Drechsler, Chief Financial Officer of the Company, certify, pursuant to 18 USC. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2003, that:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Andrew T. Drechsler

Andrew T. Drechsler
Chief Financial Officer
(Principal Financial and Accounting Officer)

February 25, 2016

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Insmed Incorporated 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 Form 10-K), irrespective of any general incorporation language contained in such filing.

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