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, 2012

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.)**
9 Deer Park Drive, Suite C **Monmouth Junction, NJ 08852**	
(Address of principal executive offices)	**(732) 438-9434** **(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 Capital 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, 2012, was $72.7 million (based on the closing price for shares of the registrant's Common Stock as reported on the Nasdaq Capital 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 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 28, 2013, there were 31,563,278 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 2013 Annual Meeting of Shareholders to be filed with the Securities and Exchange Commission no later than 120 days, or April 30, 2013, after the registrant's fiscal year ended December 31, 2012, and to be delivered to shareholders in connection with the 2013 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, ARIKACE and IPLEX are registered 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 include, but are not limited to: our ability to complete development of, receive regulatory approval for, and successfully commercialize ARIKACE®; 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") 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 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 and amount 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.

Forward-looking statements are based upon our current expectations and beliefs, and involve known and unknown risk, 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. 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 biopharmaceutical company focused on developing and commercializing inhaled therapies for patients battling serious lung diseases that are often life threatening. Our lead product candidate, ARIKACE ® or liposomal amikacin for inhalation, is an inhaled antibiotic treatment that delivers a proven and potent anti-infective directly to the site of serious lung infections to improve the efficacy, safety and convenience of this therapeutic approach for patients.

Currently, we are conducting clinical trials of ARIKACE for two initial indications in orphan patient populations: a phase 3 clinical trial in cystic fibrosis (CF) patients who have lung infections caused by *Pseudomonas aeruginosa* (*Pseudomonas*) and a phase 2 clinical trial in patients who have lung infections caused by non-tuberculous mycobacteria (NTM). Our strategy is to continue to develop ARIKACE for additional indications beyond *Pseudomonas* in CF and NTM. Our primary development focus is to obtain regulatory approval for ARIKACE in these two initial indications and to prepare for commercialization initially in Europe and Canada and eventually in the United States (US). If approved, ARIKACE will be the first once-a-day inhaled antibiotic treatment option available for these CF and NTM indications. The following table summarizes the current status of ARIKACE development.

Product Candidate/Target Indications	Status
ARIKACE *Pseudomonas aeruginosa* lung infections in CF patients	Phase 3 clinical trial in Europe and Canada was fully enrolled in November 2012. Clinical results are currently expected in mid-2013. Two-year open-label extension study is enrolling and is expected to be completed in late 2014. Granted orphan drug designation in Europe and the US. If approved, ARIKACE would be the only once-a-day treatment for *Pseudomonas* lung infections in CF patients. If approved, we plan to commercialize ARIKACE ourselves in Europe and in Canada. We will evaluate our plans for CF in the US after reviewing the phase 3 results from our study in Europe and Canada
ARIKACE Non-tuberculous mycobacteria (NTM) lung infections	Phase 2 study in the US and Canada began enrolling in June 2012. Clinical results are currently expected in Q4 2013. We expect to commence a limited compassionate use program in the second half of 2013. If approved, ARIKACE would be the first approved inhaled antibiotic treatment for NTM lung infections. If approved, we plan to commercialize ourselves initially in the US and eventually in Europe and in Canada.
ARIKACE *Pseudomonas aeruginosa* and other susceptible organisms causing lung infections in non-CF bronchiectasis patients	Phase 2 study in the US completed. Granted orphan drug designation in the US. We expect to evaluate development and commercialization strategies when we complete our Phase 3 study in CF patients with *Pseudomonas* lung infections and Phase 2 study in patients with NTM infections.

ARIKACE is considered a new molecular entity (NME) by the United States Food and Drug Administration (FDA) primarily due to its proprietary liposomal technology. For a description of our liposomal technology, see "—Our Proprietary Liposomal Technology." The key active ingredient, amikacin, is an FDA-approved antibiotic with proven efficacy in the treatment of a broad range of gram-negative infections, including *Pseudomonas* and NTM. ARIKACE is in the aminoglycoside class of antibiotics.

ARIKACE is differentiated by our proprietary advanced liposomal technology, which is designed specifically to enhance the delivery profile, safety and efficacy of pharmaceuticals delivered to the lung via inhalation. We believe ARIKACE provides potential improvements over existing treatments for these indications. In phase 2 studies in CF patients with *Pseudomonas* lung infections, ARIKACE demonstrated improved patient lung function during treatment as well as in the period following treatment (the "off-treatment" period). In a phase 2 open label extension study, ARIKACE also demonstrated statistically significant effectiveness for up to 56 days off-treatment over multiple treatment cycles.

If approved for CF patients with *Pseudomonas* lung infections, we expect ARIKACE would be the first inhaled antibiotic to be approved for once-daily administration in this indication. If approved for NTM patients, we expect ARIKACE would be the first and only approved treatment for the treatment of NTM lung infections. ARIKACE has been granted orphan drug designation for CF patients who have *Pseudomonas* lung infections in both the European Union (EU) and the US. We plan to file for orphan drug designation for NTM lung infections in the US and Europe in 2013.

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 pharmaceutical company focused on the development of differentiated and innovative inhaled pharmaceuticals for the site-specific treatment of serious lung infections. Our integration with Transave was completed in 2011. Our current operations are based on the technology and product candidates historically developed by Transave.

Our Strategy

Our strategy is to focus on the development and commercialization of innovative inhaled therapies for patients who are battling serious orphan lung diseases. While we believe that ARIKACE has the potential to treat many different diseases, our attention is initially focused on regulatory approval and commercialization preparation for our two initial indications, CF patients with *Pseudomonas* lung infections and patients with NTM lung infections, in Europe, Canada and the US. Our current priorities are as follows.

- Actively pursue new drug filings to secure approval for ARIKACE in Europe, Canada and the US;
- Expand our product supply chain in support of clinical development and if approved, commercialization;
- Prepare for commercial launch in Europe, Canada and the US; and
- Attempt to source promising late stage or commercial products that we believe are complementary to ARIKACE and our core competencies.

To support these priorities, we plan to complete our ongoing European and Canadian registrational phase 3 clinical study of ARIKACE in CF patients with *Pseudomonas* lung infections and advance our regulatory filings. We also plan to complete enrollment in our US and Canadian phase 2 clinical study of ARIKACE in patients with NTM lung infections and we intend to pursue a limited compassionate use program in the US for other patients with NTM lung infections. We plan to scale up manufacturing, work towards implementation of second source suppliers, and implement supply and quality agreements in preparation for commercialization of ARIKACE. We also intend to continue to work closely with PARI Pharma GmbH (PARI), the manufacturer of our drug delivery nebulizer we expect the ARIKACE treatment to use, to address our commercial supply needs. We also intend to commence the build out of our commercial infrastructure in preparation for potential commercial launches in Europe, Canada and the US. We will continue to evaluate opportunities for additional products through various business development channels.

Product Candidates

Our lead product candidate, ARIKACE or liposomal amikacin for inhalation, is a once-a-day inhaled antibiotic treatment engineered to deliver a proven and potent anti-infective directly to the site of serious lung infections. There are two key components of ARIKACE: the liposomal formulation of the drug and the nebulizer device through which ARIKACE is inhaled through the mouth and into the lung. The nebulizer technology is owned by PARI, but we have exclusive access to this technology, which is specifically developed for the delivery of our liposomal encapsulation of amikacin, through our licensing agreement with PARI. Our proprietary liposomal technology and nebulizer are designed specifically for delivery of pharmaceuticals to the lung and provides for potential improvements to existing treatments. We believe that ARIKACE has potential usage for at least two orphan patient populations with high unmet need: CF patients who have *Pseudomonas* lung infections and patients who have NTM lung infections. We estimate the combined global market potential for these two orphan indications to be approximately $1 billion.

ARIKACE has the potential to be differentiated from other marketed drugs for the treatment of chronic lung infections by improving efficacy, safety and patient convenience. We believe efficacy may be improved due to the ability of ARIKACE to deliver high, sustained levels of amikacin directly to the lung and to the specific site of the underlying infection. We also believe that ARIKACE may have increased durability of effect, benefiting patients when off treatment. In addition, the inhalation delivery of ARIKACE may reduce the potential for adverse events such as ototoxicity (hearing loss, ringing in the ears and/or loss of balance) and nephrotoxicity (toxicity to the kidneys), as compared with intravenous (IV) administration of amikacin. If approved, we expect that ARIKACE will be administered once daily for approximately 13 minutes via inhalation using the eFlow ® Nebulizer System, which has been optimized specifically for ARIKACE by PARI. We believe that this nebulizer system will reduce treatment time or dosing frequency, as compared with the currently marketed inhaled antibiotics, which require dosing two to three times daily with treatment times ranging from approximately 10 to 40 minutes per day. By easing the patient's treatment burden we believe that ARIKACE can potentially improve patient compliance, which we believe may in turn lead to a reduction in the development of antibiotic resistance and, ultimately, lead to clinical benefit.

We believe that ARIKACE may provide: (1) improved efficacy resulting from sustained deposition of drug in the lung and improved ability to reach the site of infection (for CF *Pseudomonas* infections, this means penetration of biofilm and facilitated drug release by factors that are secreted by the bacteria, and for NTM, this means enhanced uptake into macrophages, where NTM often grows); (2) decreased adverse events and improved tolerability as compared with amikacin delivered intravenously; and (3) reduced dosing frequency or treatment time as compared to existing products.

ARIKACE for CF Patients with *Pseudomonas* Lung Infections

Disease

CF is an inherited chronic disease that is often diagnosed before the age of two. CF occurs primarily in individuals of central and western European origin. CF affects roughly 70,000 children and adults worldwide, including 30,000 children and adults in the US (Cystic Fibrosis Foundation Patient Registry, 2011) and 35,000 patients in Europe (Hoiby, BMC Medicine, 2011, 9:32). There is no cure for CF.

Despite extensive treatment with multiple antibiotics, improved nutrition, and other treatments, life expectancy of a CF patient is only about 37 years (Cystic Fibrosis Foundation Patient Registry, 2011). Median predicted age of survival is calculated using life table analysis (as calculated by actuaries) given the ages of the patients in the registry and the distribution of deaths. Using this calculation, half of the people in the patient registry are expected to live beyond the median predicted survival age, and half are expected to live less than the median predicted survival age.

Among other issues, CF causes thick, sticky mucus to develop in and clog the lungs. This creates an ideal environment for various pathogens, such as *Pseudomonas* , to colonize and lead to chronic infection of the lung, inflammation and progressive loss of lung function. In fact, chronic bronchial infections with *Pseudomonas* are a major cause of morbidity and mortality among patients with CF. Once a CF patient acquires a *Pseudomonas* infection, it is difficult to eradicate. The current, best available treatment is chronic administration of antibiotics to suppress the bacteria, reduce inflammation and preserve lung function for as long as possible. The rate of infection with *Pseudomonas* in CF patients increases with age. It is estimated that 70% of adult CF patients have chronic infection due to *Pseudomonas* (CFF Patient Registry, 2011). A study reported in the *Journal of Cystic Fibrosis* (Liou, 2010) found that deterioration in lung function of CF patients is the main cause of death and that, despite best efforts, lung function declines by 1% to 3% annually.

Current Treatment Options and Limitations

CF therapy significantly impacts patients' quality of life. Patients generally receive extensive antibiotic treatments, which can be delivered via the oral, intravenous and inhaled routes. Some CF patients spend up to three hours per day taking medications and other treatments, including inhaled antibiotics, and often face the burden of taking in excess of 20 pills per day. All currently approved inhalation treatments for *Pseudomonas* lung infections require two- to three-times a day dosing.

Antibiotics delivered via inhalation are part of the standard treatment for CF patients with *Pseudomonas* lung infections and are generally thought to be a way to deliver more active drug directly to the site of infection compared with other routes of administration. Specifically, the most used treatment in the US for the management of chronic *Pseudomonas* infection in subjects with CF is suppressive therapy with 300 mg twice daily of Tobi inhaled solution. Tobi, which is approved by the FDA for CF patients ages six years and above with a FEV1 (forced expiratory volume in 1 second) of 25%-75%, has been sold in the US since January 1998. A 1999 study reported that Tobi, 300 mg, administered twice a day for cycles of 28 days followed by 28-days-off treatment was shown to reduce *Pseudomonas* colony counts, increase FEV1 percent predicted, reduce hospitalizations and decrease additional antibiotic use (Ramsey et al., 1999). High levels of tobramycin can be attained in the lung with relatively low systemic exposure with inhaled drug compared to intravenous tobramycin. However, patients using Tobi must be dosed twice a day for approximately 15 to 20 minutes of inhalation session per dose for a total of approximately 30 to 40 minutes per day. Recent data show that the effect of Tobi on pulmonary function has lessened since its introduction into the marketplace more than a decade ago (Konstan et al., Journal of Cystic Fibrosis, January 2011, and Assael et al., 34 th European Cystic Fibrosis Society Conference, Poster 86, June 2011). In addition, according to information presented at a FDA advisory panel, resistance to Tobi has increased 85% in the ten-year period from 1999 to 2009 (FDA advisory panel US-FDA-AIDAC for Tobi-Podhaler, September 2012).

Market

We estimate that the global market for the treatment of *Pseudomonas* lung infections in CF patients is approximately $500 million. We believe this market is being driven by physicians' desire to maintain the lung function of CF patients, which continues to decline in many patients despite extensive treatment with current therapies including currently approved inhaled antibiotics. We believe that the following additional factors may lead to further market growth:

- Better patient adherence to physician prescribed regimens resulting from more convenient (less frequent and less time consuming) treatments;
- Physicians initiating treatment with inhaled antibiotics earlier for patients with *Pseudomonas* in their lungs;
- CF patients living longer;
- Physicians moving to a different antibiotic every other month as opposed to giving patients off-treatment holidays on alternate months; and
- The standard of care in the rest of the world continuing to advance closer to that in the EU and the US.

Potential Benefits of ARIKACE for CF Patients with Pseudomonas Lung Infections

Potential for Improved Compliance

We believe ARIKACE may facilitate better patient compliance, which may result in better effectiveness and thereby differentiate it from other marketed drugs for the treatment of chronic *Pseudomonas* lung infections in CF patients. The most used treatment in the US for the management of chronic *Pseudomonas* infection in subjects with CF is suppressive therapy with 300 mg twice daily of Tobi inhaled solution. Tobi is administered twice daily for approximately 15 to 20 minutes per treatment for a daily total of approximately 30 to 40 minutes per day for 28 days followed by a 28-day-off period. This cycle of "on and off" treatment is repeated in a chronic pattern. We anticipate that ARIKACE will be administered once daily for approximately 13 minutes per day for 28 days followed by a 28-day off-drug period. We believe that any inhaled treatment that reduces the treatment burden on a CF patient could represent a significant improvement in the patient's quality of life and result in improved compliance, as well as reduce the development of antibiotic resistance.

Potential for Increased Efficacy

We believe ARIKACE has the potential to deliver high levels of amikacin directly to the site of bacteria in the lung for a sustained period of time, which we expect would differentiate it from other marketed drugs for the treatment of chronic *Pseudomonas* lung infections in CF patients. Current inhaled antibiotics are commonly used as standard treatments for CF patients with *Pseudomonas* lung infections and generally are thought to be a way to deliver more drug directly to the site of infection as compared with other methods of delivery. However, CF patients seldom clear the *Pseudomonas* permanently from their lungs, in part because of the thick sticky mucus these patients produce in their lungs, and often become chronically infected despite existing antibiotic treatments. All existing aminoglycoside antibiotics, including tobramycin and amikacin, are positively charged and tend to bind to the negative surfaces of mucus and the biofilm. In contrast, we have designed ARIKACE to be a neutrally charged liposome, which has been shown in laboratory studies, to penetrate both CF mucus and a *Pseudomonas* biofilm. This means that ARIKACE may reach the site of the *Pseudomonas* infection in CF patients' lungs more efficiently than the other currently available aminoglycoside antibiotics, including currently available inhaled antibiotics.

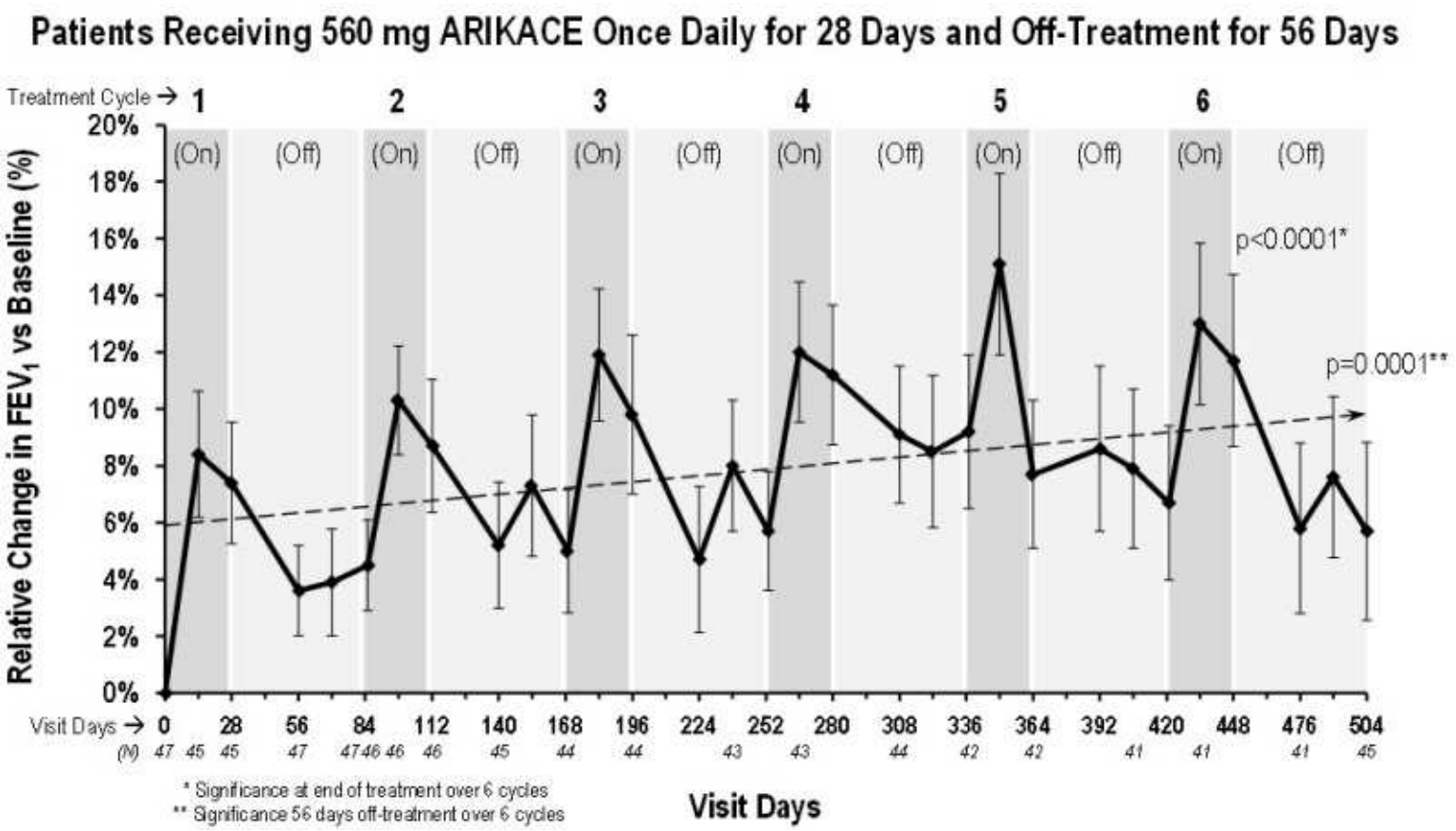
In addition, ARIKACE has demonstrated a prolonged half-life in animals' lungs. We expect that liposomes manufactured using our proprietary liposomal technology will provide sustained benefits to the lung by maintaining the drug in the lung longer. One important measure of the effectiveness of antibiotics is the maintenance of anti-bacterial drug levels in the lung above the minimum inhibitory concentration.

We believe these attributes of ARIKACE most likely contributed to the improved lung function relative to baseline that was observed during treatment periods and sustained during off treatment periods in our phase 2 clinical trials in CF patients.

Potential for Increased Durability of Effect

We believe ARIKACE may be further differentiated from other marketed drugs for the treatment of chronic *Pseudomonas* lung infections in CF patients due to improved lung function during longer off-treatment cycles. Typically an inhaled antibiotic is given to CF patients with chronic *Pseudomonas* lung infections for 28 days followed by a 28-day off-treatment cycle, which is often repeated chronically or for the rest of a patient's life. During phase 2 studies ARIKACE demonstrated statistically significant and clinically meaningful improvement in pulmonary function throughout the 28-day treatment period, and such improvement was sustained during the 28-days off treatment period.

In addition, during an open-label phase 2 extension trial (TR02-105), CF patients using ARIKACE demonstrated sustained efficacy in lung function improvement during a 28-day treatment period and 56-day off-treatment period across multiple cycles of therapy as compared to baseline. In this clinical study, ARIKACE produced an improvement in lung function that was sustained over six cycles totaling approximately 17 months. During the off-treatment periods for this study, approximately 50% to 70% of the benefit achieved during the on-treatment periods was sustained at the end of the off-treatment periods. To our knowledge, no other inhaled antibiotic has shown sustained improvement in lung function at the end of a 56-day off-treatment period. The following graph summarizes the results of our open-label Phase 2 extension trial:



Potential for Increased Safety

We believe ARIKACE has the potential to be safer than intravenous delivery of aminoglycosides. *Pseudomonas* is susceptible to several broad spectrum antibiotics, notably aminoglycosides. Some examples of aminoglycoside antibiotics include tobramycin and amikacin. Studies found that aminoglycosides are an important class of antibiotics for the treatment of *Pseudomonas* lung infections in CF patients because of their broad antimicrobial activity and concentration dependent bactericidal activity (Lacy et al., 1998; Lortholary et al., 1995; Zembower et al., 1998). Intravenous antibiotics were originally used for treatment of chronic infections associated with CF and are still used for pulmonary exacerbations. Studies report that ototoxicity and nephrotoxicity are common adverse events associated with the use of intravenous aminoglycosides and these effects are related to plasma drug levels (Mingeot-Leclercq and Tulkens, 1999).

There are two main obstacles to effective and safe treatment of CF:

- Drug Resistance. High-level multi-drug resistance complicates eradication of such strains from the bronchial secretions of CF patients. *Pseudomonas* lung infections are commonly treated using aminoglycoside antimicrobial agents, such as amikacin and tobramycin. However, due to drug resistance, significantly higher concentrations of these drugs above the minimum inhibitory concentration are required at the site of infection. The intravenous dosage levels required to achieve such exposures can be nephrotoxic and ototoxic.
- Limited Penetration. There is limited penetration into the sputum/biofilm matrix by aminoglycoside antibiotics. The antibiotics are positively charged and the biofilm is negatively charged. As a result the antibiotics bind to the biofilm and the availability of the drug at the location of the microorganism is suboptimal. We believe that our proprietary liposomal technology will result in localized targeting of drugs, leading to increased availability of the drug at the location of the microorganism, while significantly reducing drug exposure at non-disease sites throughout the body and reducing the occurrence of systemic drug-related toxicity.

Current Clinical Program

We are conducting a registrational phase 3 clinical study of ARIKACE for CF patients with *Pseudomonas* lung infections in Europe and Canada. The phase 3 trial includes 302 patients and is a 1:1 randomized trial comparing ARIKACE 560 mg, delivered once daily for approximately 13 minutes via the eFlow Nebulizer System, to Tobi , which is delivered twice daily approximately 15 minutes per treatment for a daily total of approximately 30 minutes per day. The first patient in this trial was dosed in April 2012, and the trial met target enrollment in November 2012. The study's primary endpoint is relative change in forced expiratory volume in one second (FEV1) from baseline measured after the completion of three cycles, each comprising a 28-day on-treatment and a 28-day off-treatment period. Approximately 260 patients are required to demonstrate non-inferiority at an agreed-upon margin with 80% power. Secondary endpoints for the study include change in pulmonary function, time to and the proportion of patients experiencing pulmonary exacerbation, the time elapsed to first antipseudomonal antibiotic treatment for pulmonary exacerbation, time to and number of hospitalizations, reduction in bacteria as measured by reduction in colony forming units, change in patient-reported symptoms and evaluation of safety and tolerability. We previously agreed with the European Medicines Agency (EMA) on the study design. We currently expect to announce clinical results from the phase 3 trial in mid-2013.

In addition, patients completing the initial 24 week phase 3 study will have the option to enroll in a two-year open-label safety study. The patients in this study will receive ARIKACE for a two year period, using the same cycles of a 28 day on-treatment period and a 28 day off-treatment period.

Development History

Nonclinical evaluations of ARIKACE in relation to *Pseudomonas* lung infections indicate:

- High concentrations of drug are deposited in the lung, and high levels are maintained for prolonged periods, with low serum concentrations,
- ARIKACE penetrates CF sputum and *Pseudomonas* biofilm,
- ARIKACE exhibits antipseudomonal activity in *in vitro* and *in vivo* models, including against resistant isolates, and
- virulence factors secreted by *Pseudomonas* facilitate the release of amikacin from ARIKACE.

Our predecessor liposomal amikacin formulations for inhalation were evaluated in a series of phase 1 clinical studies involving healthy volunteers and CF patients with *Pseudomonas* lung infections. The current formulation of ARIKACE was evaluated in phase 2 clinical studies in CF patients with *Pseudomonas* lung infections. We completed two randomized, placebo-controlled phase 2 studies with ARIKACE in 105 CF patients with chronic *Pseudomonas* lung infections in Europe and the US. In these studies, patients in the ARIKACE 560 mg cohort demonstrated statistically significant and clinically meaningful improvement in lung function throughout the 28-day on-treatment period compared with placebo. In addition, the improvement in lung function that was achieved at the end of the 28-day on-treatment period was sustained during the 28-day off-treatment period and was statistically significantly better than placebo.

In a separate follow-on open-label, multi-cycle clinical trial conducted in Europe, ARIKACE was given at a dose of 560 mg once daily via an eFlow Nebulizer System for six cycles which consisted of a 28-day on-treatment and 56-day off-treatment period, which is double the standard 28-day off-treatment period. In this clinical study, ARIKACE produced a statistically significant improvement in lung function that was sustained over the six cycles (approximately 17 months). In addition, approximately 50% to 70% of the benefit achieved during the 28-day on-treatment periods was sustained at the end of the 56-day off-treatment periods. In other words, ARIKACE demonstrated sustained efficacy in lung function improvement during the treatment and off-treatment periods across multiple cycles of therapy. To our knowledge, no other inhaled antibiotic has shown sustained improvement in lung function at the end of a 56-day off-treatment period. In addition, ARIKACE was well tolerated with overall adverse events reported as consistent with those expected in a population of CF patients receiving other inhaled medicines.

In August 2011, we announced that the FDA placed a clinical hold on our phase 3 trial for ARIKACE in CF patients with *Pseudomonas* lung infections, which was lifted in May 2012. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical trial or suspend an ongoing clinical trial. The FDA based its clinical hold decision on an initial review of the results of a long-term rat inhalation carcinogenicity study with ARIKACE. When rats were given ARIKACE daily by inhalation for two years, 2 of the 120 rats receiving the highest dose had a single lung tumor. These rats received ARIKACE doses that were within two-fold of those in clinical studies (normalized on a body surface area basis or a lung weight basis). ARIKACE was not associated with changes that may lead to tumors in shorter-term studies in animals. Additionally, ARIKACE was not shown to be genotoxic in our standard series of tests. The relevance of the observed rat tumors to the use of ARIKACE in humans is not known.

In connection with the FDA's decision to lift the clinical hold for all disease indications, we agreed to conduct a 9 month dog inhalation toxicity study of ARIKACE. In late January 2013, we concluded the 9 month dosing phase of the dog inhalation toxicity study. Consistent with the design of the study, we conducted a review of the lung and kidney tissues in the first group of dogs upon completion of the 9 month dosing. Additionally, a group of dogs designated for the recovery period of the study continue in the off drug observation period. As agreed with the FDA, an unaudited interim report of the findings from the first group of dogs that completed 9 months of dosing was recently submitted to the FDA. In summary, this report stated that the lung macrophage response in the first group of dogs was similar to that seen in our previous 3 month dosing dog study, and there was no evidence of neoplasia, squamous metaplasia or proliferative changes. We also informed the FDA that we are planning the recovery period to be 3 months as there were no findings of note at the end of the 9 month dosing phase. We will file the final report for both groups of dogs with the FDA once data from the 3 month recovery period is available.

We expect to reevaluate our plans regarding a US phase 3 clinical trial in CF patients with *Pseudomonas* lung infection after we receive the results from the ongoing phase 3 clinical trial in Europe and Canada.

Strategy for Commercialization

We currently plan to retain marketing rights for ARIKACE in Europe, Canada and the US. We believe ARIKACE will require a limited commercial infrastructure in these regions because of the small focused nature of the potential physician prescribing population for CF patients. We may license ARIKACE for certain indications outside of Europe, Canada and the US. In 2013, we plan to commence preparations for the potential commercialization of ARIKACE in Europe and Canada, including hiring a chief commercial officer and several other positions to support sales and marketing efforts.

ARIKACE for Patients with NTM Lung Infections

Disease

Non-tuberculous *mycobacteria*, or NTM, are organisms common in soil and water that have been associated with lung disease in select patient groups. NTM have characteristics that are similar to tuberculosis, or TB, but NTM are not contagious. Many people have NTM in their bodies, but NTM do not normally lead to an infection, perhaps because the body's immune system successfully overcomes the threat of infection. It is not completely understood why certain individuals are susceptible to NTM infections. However, the patients who become infected by NTM often are immune-compromised or have structural damage in their lungs at the time of the infection.

NTM are organisms that invade and multiply chiefly within macrophages. They are characteristically resistant to most antibiotics. NTM lung infections are chronic, debilitating and progressive and often require lengthy, repeat hospitalizations. Signs and symptoms of NTM pulmonary disease are variable and nonspecific. They include chronic cough, sputum production and fatigue. Less commonly, malaise, dyspnea, fever, hemoptysis, and weight loss also can occur, usually with advanced NTM disease. Evaluation is often complicated by the symptoms caused by co-existing lung diseases. According to a study published in the *American Journal of Respiratory and Critical Care Medicine* , these conditions include chronic obstructive airway disease associated with smoking, bronchiectasis, previous mycobacterial diseases, CF and pneumoconiosis (Olivier et al. 2003).

Current Treatment Options and Limitations

There currently is no drug approved for treatment of NTM lung disease, and as a result all current drug treatments for NTM are used off-label. Patients are often treated with the same antibiotics that are used to treat TB. Such treatments usually consist of lengthy multi-drug antibiotic regimens, which are often poorly tolerated and not very effective, especially in patients with severe disease and patients who have failed prior treatments. NTM patients average 7.6 antibiotic courses per year (SDI Healthcare Database, July 2009). Treatment guidelines published in 2007 in the *American Journal of Respiratory and Critical Care Medicine* reported that few clinical trials were under way to identify treatment recommendations, and no new antibiotics had been studied for the treatment of NTM lung infections in multi-center, randomized clinical trials for many years.

Amikacin is not approved by the FDA for NTM lung infections but is often recommended as part of the standard treatment regimen for some NTM patients. It is delivered most commonly by intravenous administration and, less often, by inhalation. Because the drug is delivered for months at a time, resulting in high systemic (blood) levels of the drug, there can be considerable toxicity, including ototoxicity and nephrotoxicity, associated with intravenous treatment.

Market

The prevalence of human disease attributable to NTM has increased over the past two decades. 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 in the US in 2011 and that such cases were estimated to be growing at a rate of 10% per year. NTM is four to five times more prevalent than TB in the US (Incidence of TB from Center for Disease Control and Prevention Morbidity and Mortality Weekly Report, March 2012). In a decade-long study, researchers found that the diagnosis of NTM is increasing at approximately 8% per year and that those NTM patients over the age of 65 are 40% more likely to die than those who do not have the disease (Adjemian et al. Prevalence of Pulmonary Nontuberculous Mycobacterial Disease among Medicare Beneficiaries, USA, 1997-2007, American Journal of Respiratory and Critical Care Medicine, April 2012).

Although there are many species of NTM that have been reported to cause lung infections, ARIKACE is intended to treat two of the most common, *Mycobacterium Avium* Complex (MAC) and *Mycobacterium abscessus* (*M. abscessus*). MAC accounts for the vast majority of NTM lung infections with prevalence rates from 72% to more than 85% in the US. The reported prevalence rates for *M. abscessus* range from 3% to 11% in the US. The diagnosed prevalence of NTM species causing lung infections varies geographically with MAC rates of 25% to 55% reported in Europe. We are conducting a chart audit to more specifically quantify the incidence of NTM lung infections in both Europe and Japan. We anticipate receiving the results of this primary market research in the second half of 2013.

Potential Benefits of ARIKACE for NTM Lung Infections

If approved, ARIKACE would be the first and only approved treatment for patients battling NTM lung infections.

Potential Efficacy

We believe that ARIKACE may be effective in treating patients with NTM lung infections due to the ability of the ARIKACE liposomes to be taken up inside lung macrophages that harbor NTM. Macrophages are immune cells whose primary function includes removing foreign particles and bacteria from the lungs. NTM are taken up by and multiply inside these macrophages. Many antibiotics cannot efficiently gain access to the macrophage interior. ARIKACE liposomes, however, are designed to be internalized by lung macrophages and thereby deliver high levels of drug inside the macrophages where the NTM bacteria are located.

ARIKACE has been shown to have superior *in vitro* activity against MAC and *M. abscessus* when compared with amikacin solution (study conducted by L.E. Bermudez at Oregon State University, data on file, 2010). ARIKACE also has been shown to more effectively kill certain forms of NTM in cultured lung phagocytes as compared to soluble amikacin.

Potential Safety Profile

We believe ARIKACE has the potential to be safer than intravenous delivery of aminoglycosides. One potential benefit of ARIKACE, relative to intravenous administration of amikacin, may result from the delivery of the drug more directly to the site of disease. By delivering the drug more directly to the site of the disease, we believe non-disease sites throughout the body should be exposed to significantly less drug as compared to intravenous administration of amikacin. We believe this may reduce the potential for the occurrence of any drug-related toxicity, which is especially important with diseases like NTM that require long-term drug administration.

Potential for Improved Patient Convenience

We believe ARIKACE, if approved, could improve patient convenience by providing once-a-day dosing. According to *SDI Healthcare Database* NTM patients average 7.6 antibiotic courses and 10.2 hospital days per year, We anticipate that ARIKACE will be administered once daily for approximately 13 minutes per day for a period of 84 days for this indication. We believe that an effective inhaled treatment that improves the outcomes for an NTM patient would represent a significant benefit in the patient's quality of life.

Current Clinical Program

We are currently conducting a phase 2 clinical trial in the US and Canada for ARIKACE in adult patients with NTM lung infections. We began enrolling patients in June 2012. The phase 2 clinical trial is a randomized, placebo-controlled study of approximately 100 adult patients with recalcitrant NTM lung infections. There are two parts to the study: a randomized portion and an open-label portion.

In the randomized portion of the study, patients are screened initially to include in the study those who have NTM lung infections with persistent sputum culture for MAC or *M. abscessus* while on ATS/IDSA-guidelines-based treatment regimen for at least six months prior to screening. Patients who are NTM culture positive and meet the eligibility criteria to enroll in the study will receive, in addition to their ongoing antibiotic treatment regimen, either ARIKACE 560 mg or a placebo both delivered once daily for approximately 13 minutes via an optimized, investigational eFlow Nebulizer System.

The primary efficacy endpoint for this study is the change in mycobacterial density from baseline to the end of 84 days of treatment. At a public workshop discussion in September 2012, the FDA agreed that the microbiological end-point is an appropriate primary end-point for NTM lung disease. The study will also measure secondary endpoints, including the proportion of patients with culture conversion to negative, the time to "rescue" anti-mycobacterial drugs, the change from baseline in six-minute walk distance and oxygen saturation, the change from baseline in patient reported outcomes, and evaluation of safety and tolerability. At the conclusion of the randomized portion of the study, eligible patients will receive ARIKACE once daily for an additional 84 days during the open-label portion of the study, primarily to measure longer-term safety and efficacy. We previously agreed with the FDA on this clinical trial design. We expect results from this clinical trial in the fourth quarter of 2013.

In addition to the phase 2 clinical trial outlined above, we intend to pursue a limited compassionate use program starting in the second half of 2013. We currently anticipate this program's participants will consist of approximately 25 patients who have NTM lung infection but are not eligible for entry into our phase 2 clinical trial. We believe that clinical data collected from the experience with these patients will help regulatory authorities to evaluate ARIKACE's safety and suitability for treating NTM lung infection patients.

Development History

Nonclinical evaluations of ARIKACE in relation to NTM infections indicate: (1) High concentrations of drug are deposited in the lung, and high levels are sustained for prolonged periods, with low serum concentrations and (2) ARIKACE has *in vitro* activity that is superior to amikacin solution against different strains of NTM.

Data obtained from *in vitro* testing of ARIKACE with respect to four different strains of MAC and *M. abscessus* indicate dose response with ARIKACE and superior activity to free amikacin. We believe that the safety and efficacy data obtained from the phase 2 studies of ARIKACE in CF and non-CF patients with chronic lung disease and pulmonary infections and the non-clinical data collected to date serve as the basis for further development of ARIKACE in patients with NTM lung infections.

We received a response to our pre-IND application for ARIKACE in the treatment of NTM lung infections and submitted an IND to launch a phase 3 study of ARIKACE in CF and non-CF patients with NTM lung disease. In August 2011, prior to starting the NTM study, we announced that the FDA placed a clinical hold on our phase 3 trial for ARIKACE in patients with NTM lung infections. The clinical hold for NTM was lifted in January 2012. The FDA based its clinical hold decision on an initial review of the results of a long-term rat inhalation carcinogenicity study with ARIKACE. When rats were given ARIKACE daily by inhalation for two years, 2 of the 120 rats receiving the highest dose had a single lung tumor. These rats received ARIKACE doses that were within two-fold of those in clinical studies (normalized on a body surface area basis or a lung weight basis). ARIKACE was not associated with changes that may lead to tumors in shorter-term studies in animals. Additionally, ARIKACE was not shown to be genotoxic in our standard series of tests. The relevance of the observed rat tumors to the use of ARIKACE in humans is not known. The FDA requested we conduct a phase 2 clinical trial, instead of our previously agreed upon phase 3 clinical trial in adult NTM patients, to provide proof-of-concept efficacy and safety data for ARIKACE in NTM patients. Despite the change in status from phase 3 to phase 2, the study design and target enrollment did not change.

Strategy for Commercialization

We currently plan to retain marketing rights for ARIKACE in Europe, Canada and the US. Given the current lack of approved treatments for NTM lung infections, we believe we will immediately have a strong market position if ARIKACE is approved for commercialization in the NTM indication. We believe ARIKACE will require a limited commercial infrastructure in these regions because of the small focused nature of the potential physician prescribing population for NTM patients. We may seek to license ARIKACE for certain indications outside of Europe, Canada and the US. As discussed above, in 2013, we plan to commence preparations for the potential commercialization of ARIKACE, including hiring a chief commercial officer and several other positions to support sales and marketing efforts. We believe there will be substantial carryover between lung specialist physicians who treat CF patients with pseudomonas lung infections and those who have NTM lung infections thereby allowing us to leverage our commercial infrastructure across both indications.

ARIKACE for Non-CF Bronchiectasis Patients with *Pseudomonas* Lung Infections

Disease

We believe ARIKACE has the potential to be used to treat non-CF bronchiectasis characterized by *Pseudomonas* lung infections. However, we are currently concentrating our development efforts on the treatment of *Pseudomonas* lung infections in CF patients and patients with NTM lung infections. We will evaluate our development and commercialization strategies for this indication when we complete our Phase 3 study in CF patients with *Pseudomonas* lung infections and Phase 2 study in patients with NTM infections.

Non-CF bronchiectasis is a serious pulmonary condition characterized by localized, irreversible enlargement of the bronchial tubes. Accumulation of mucus in the bronchi leads to frequent infections, which causes inflammation and further reduces lung function. Patients evolve to a chronic inflammation-infection cycle. Disease burden has primarily been linked to productive cough and high levels of sputum production.

Market

It is estimated that there are more than 250,000 non-CF bronchiectasis patients in the US (SDI Innovations in Healthcare Analytics, 2008), of which approximately 30% of non-CF bronchiectasis patients are infected with *Pseudomonas* (Wilson, C.B., et al., Eur Respir, 1997, 10(8):1754-1760); Nicotra, M.B., et al., Chest, 1995 108(4):955-961). Currently there are no approved antibiotics for this indication. When bronchiectasis patients become infected with *Pseudomonas* , they tend to have more frequent exacerbations and hospitalizations and are more frequent users of antibiotics.

Development Program

ARIKACE was granted orphan drug status in the US for the treatment of bronchiectasis in patients with *Pseudomonas* or other susceptible pathogens.

In May 2009 we completed our randomized, placebo controlled US phase 2 study (TR02-107) of ARIKACE in the treatment of chronic *Pseudomonas* infection in non-CF patients with bronchiectasis. In the study, 64 study subjects were randomized (1:1:1) to receive ARIKACE 280 mg, ARIKACE 560 mg or a placebo on a daily basis during a 28-day on-treatment period. The subjects completed follow-up assessments at the end of a 28-day off-treatment period. This study provided an initial evidence of safety, tolerability and clinically meaningful improvement in pulmonary function throughout the on-treatment period in the treatment of chronic *Pseudomonas* infection in non-CF patients with bronchiectasis.

In the study both ARIKACE 280 mg and ARIKACE 560 mg were well tolerated. The adverse events experienced by patients during the study were consistent with underlying chronic lung disease in bronchiectasis patients. There was no evidence of renal toxicity or ototoxicity. Patients in the 560-mg cohort appear to have a slightly higher frequency of dry cough post administration than patients in the 280 mg cohort. Cough was of short duration and self-limiting. One patient discontinued treatment due to dysphonia (hoarseness or difficulty speaking) and cough.

There was a statistically significant reduction in *Pseudomonas* density observed in the 560 mg ARIKACE cohort relative to the placebo cohort. Patients receiving ARIKACE experienced fewer pulmonary exacerbations at a rate of 4.7%, as compared to 10.5% in those receiving placebo. No patients in the ARIKACE cohorts required anti- *Pseudomonas* rescue treatment, whereas 15% of patients in the placebo cohort required treatment. Hospitalization from any cause occurred at a 5.3% rate for patients in the placebo cohort, as compared to a 2.3% rate for patients in the ARIKACE cohort. Patients receiving ARIKACE achieved improvements in patient respiratory symptoms and quality of life assessments compared with patients receiving placebo.

Although we believe there is an opportunity to develop ARIKACE for non-CF bronchiectasis, we do not intend to initiate further clinical studies with respect to a non-CF bronchiectasis indication until we have completed additional clinical studies for CF patients with *Pseudomonas* lung infections and for patients with NTM lung infections. Following those studies, we will evaluate whether to develop ARIKACE further for non-CF bronchiectasis.

Our Proprietary Liposomal Technology

We have designed our liposomal technology specifically for use in delivering pharmaceuticals to the lung. Drugs deposited in the lung typically have short residence times, from minutes to a few hours, which is problematic for treating lung conditions where maintaining high concentrations locally in the lung for long periods of time is required. We believe our technology provides for potential improvements over the conventional inhalation method for delivering pharmaceuticals to the pulmonary system. These potential advantages include improvements in efficacy, safety and patient convenience.

Liposomes are microscopic membrane shells that contain water. Liposomes usually have a single membrane but can also be designed to have several membrane layers. These layers can be arranged like the layers of an onion or like bubbles inside of larger bubbles. In all cases, there is water in the liposome’s core and between each layer. In a liposome drug delivery system, the drug is contained in the liposome and the liposomes are administered to the patient during treatment. Water soluble drugs are located in the liposome’s water core, and drugs that do not dissolve in water are located in or associated with the membrane layers.

For ARIKACE

ARIKACE liposomes are less than 0.3 microns in mean diameter and contain amikacin in the water interior in a very high concentration. These liposomes are efficient delivery systems, and we designed ARIKACE liposomes for inhalation therapy. Our liposomes are highly compatible with lung tissue because they are formed using neutral lipids identical to those found naturally in the lung. The liposomes maintain drug in the lung and thus provide sustained delivery to the lung, which may be important in treating certain bacterial infections that have a significant pulmonary component.

Charge-Neutral Liposomes

We believe neutrally charged liposomes may enable greater penetration into the mucus and biofilm, thereby providing higher drug concentrations to kill bacteria which produce the biofilm. The materials found in a patient's mucus have negative charges, and biofilms that are produced by bacteria to protect themselves also have negative charges. Because opposite charges attract each other, positively charged antibiotics, like amikacin, bind to the negatively charged compounds on the surfaces of the mucus and biofilm. This binding prevents effective penetration of positively charged antibiotic drugs into the spaces in which the bacteria are located. Specifically, in the case of Pseudomonas lung infections in CF patients, these barriers are the patient’s own sticky mucus and bacteria’s protective biofilm. In the case of NTM, the barrier to effective treatment is in gaining access to the interior of infected macrophages. ARIKACE liposomes are effective delivery systems that penetrate these barriers and provide high levels of drug in the lung for a long time.

Potential for Increased Efficacy and with Low Drug Toxicity

A potential benefit of our inhalation drug delivery technology over systemic delivery of the same drug may be enhanced efficacy as a result of greater amounts of the drug being delivered directly to the site of disease. With higher localized antibiotic concentrations bacterial infections are more readily treated. Another advantage of localized targeting of drugs using this unique delivery system is that non-disease sites throughout the body are exposed to significantly less drug. We believe this reduces the potential for the occurrence of drug-related toxicity.

High-Efficiency Drug Encapsulation

We have designed our liposomes to encapsulate very high concentrations of drug into relatively small liposome structures. According to pre-clinical models, this efficiency allows our compact, drug-laden liposomes to physically penetrate bacteria-generated biofilms. Further, we have found that drug is released from the liposomes by disruptive factors secreted by *Pseudomonas* , which we believe will cause liposomes to release their drug contents near to where the bacteria reside in the lungs.

Endogenous Lipid Excipients

We believe the ability to release drug contents in proximity to the bacteria may reduce the chance of systemic adverse reactions. The lipid components of our compounds are the same as those found naturally in the lung, which may ensure a more natural metabolism and clearance than other drug delivery systems such as particles comprised of man-made polymers containing drug.

Our liposomal formulation is key to both the retention of amikacin in the lung, which allows once-a-day dosing, and the ability of ARIKACE to gain close access to bacteria either within a biofilm, as in the case in CF patients, or within infected macrophages, as in the case of NTM patients. It is localization near the bacteria that may improve efficacy by allowing high concentrations of drug to be delivered where it is needed most.

With a neutral surface charge and small size, ARIKACE liposomes are able to effectively penetrate the thick CF mucus and the bacteria's protective biofilm, both of which we believe restrict the availability of unencapsulated aminoglycosides such as tobramycin and amikacin. ARIKACE liposomes are also readily taken up by immune cells in the lung (alveolar macrophages) that "eat" inhaled particles. When NTM infects these immune cells, it is usually sheltered against attack from external antibiotics, but with ARIKACE, the uptake of the liposomes allows the drug to get inside these cells to attack the organisms.

For Other APIs

We believe that our liposomal technology can be used for the successful delivery of other low molecular weight products as well as high molecular weight compounds such as peptides, proteins and genes. Our unique lipid-based delivery systems are not dependent on the inhalation device and can be designed to be administered either as a nebulized aerosol spray or as a dry powder.

Optimized eFlow Nebulizer System

If approved for commercialization, we expect that ARIKACE will be administered once daily via inhalation using an eFlow Nebulizer System, optimized specifically for ARIKACE by PARI, a third-party vendor. For additional information about PARI and our contractual relationship with PARI, see "—Manufacturing" and "—License and Collaboration Agreements."

The optimized eFlow Nebulizer System is a medical device that uses PARI's patented eFlow technology to enable highly efficient delivery of inhaled medication, also called aerosolization, including liposomal formulations via a vibrating, perforated membrane that includes thousands of specially designed laser-drilled holes, which aids the delivery of ARIKACE to the lung. We believe the optimized eFlow Nebulizer System is state of the art and highly efficient. The eFlow Nebulizer System delivers a very high density of active drug, in a precisely defined and controlled droplet size, with a high proportion of respirable droplets delivered in a relatively short period of time. In addition, the eFlow Nebulizer System has a quiet mode of operation, is small in size, light weight and provides for optional battery-powered operation. We believe that using the eFlow Nebulizer System to deliver ARIKACE will reduce treatment time and ease the patient's treatment burden and thereby potentially improve patient compliance. We believe that improved compliance with the prescribed treatment regimen may lead to a reduction in the development of antibiotic resistance by increasing the exposure of the infection to the minimum inhibitory concentration of antibiotic and therefore may ultimately lead to clinical benefit.

MANUFACTURING

The ARIKACE used in our clinical studies is manufactured for us by Althea Technologies, Inc., a third-party contract manufacturing organization in the US. Althea manufactures ARIKACE using the technology developed and optimized by us. We and Althea both must comply with applicable FDA regulations relating to the FDA's current good manufacturing practices (cGMP) regulations. The cGMP regulations include requirements relating to the organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. We believe Althea's facilities meet cGMP requirements for the sterile manufacturing of finished ARIKACE product. We are working with Althea to develop commercial production capabilities for AIRKACE. We are also evaluating other potential contract manufacturers for ARIKACE. Our agreement with Althea provides for a term expiring July 2014, subject to an earlier termination upon the provision of 180 days' notice by either party, or in the event of an uncured material breach, certain bankruptcy or liquidation events, or upon the occurrence of certain other specified termination events..

The eFlow nebulizer system is manufactured by PARI under the names PARI Pharma GmbH in Europe and PARI Respiratory Equipment, Inc., in the US. PARI manufactures eFlow nebulizer systems utilizing technology licensed, developed and optimized within its company and produces several commercially available eFlow technology based products for use in Europe, North America and other countries. PARI maintains facilities and equipment necessary to support manufacture of eFlow nebulizers for use with ARIKACE. PARI must comply with applicable governmental regulations relating to medical device production in each country of manufacture. We will continue to work with PARI to address our manufacturing needs for our clinical program and plan for commercialization. For additional information about PARI and our contractual relationships with PARI, see "—License Agreements and Collaboration Agreements."

We seek to maintain the quality of our suppliers through quality agreements and our vendor audit program.

IPLEX

In addition to the ARIKACE development program, we have a second proprietary compound, IPLEX ®, IGF-1, with its natural binding protein, IGFBP-3. IPLEX is no longer a development priority for us. We no longer have protein development capability or the in-house capability to manufacture IPLEX. Previously, under the proprietary IPLEX protein platform, we maintained an expanded access program for amyotrophic lateral sclerosis (also known as ALS or Lou Gehrig's disease) until drug supplies were exhausted at the end of 2011. It is our intention to seek licensing partners for the IPLEX development programs. In 2012, we out-licensed the IPLEX technology to Premacure Holdings AB and Premacure AB of Sweden (collectively, "Premacure") for retinopathy of prematurity indication. On March 12 2013, Shire plc announced that they acquired Premacure.

INTELLECTUAL PROPERTY

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 80 issued patents and pending patents related to ARIKACE. 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 both new inventions and improvements of existing technology 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, 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, and collaborators 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.

In the U.S., we own three Orange Book listable patents that cover the ARIKACE composition and its use in treating lung infections, including *Pseudomonas* and NTM. The three patents are U.S. Patent No. 7,544,369 (expires June 6, 2025), U.S. Patent No. 7,718,189 (expires June 6, 2025), and U.S. Patent No. 8,226,975 (expires August 15, 2028). Seventeen patents have also issued in major foreign markets, e.g., Japan, China, and India, which cover ARIKACE and methods of using ARIKACE for treating lung infections. Twelve U.S. patent applications and nearly fifty foreign patent applications, including applications under examination in the European Patent Office, are pending that cover the ARIKACE composition and its use in treating lung infections, including *Pseudomonas* and NTM. We anticipate that we will have potential patent coverage for ARIKACE and its use in treating lung infections, including *Pseudomonas* and NTM, through at least February 2029, which includes an additional six months of pediatric exclusivity.

Through our agreements with PARI, we have license rights to U.S. and foreign patents and applications that cover the eFlow Nebulizer System medical device. We currently have rights to use the nebulizers in clinical trials and, pursuant to its agreements with us, PARI has agreed to negotiate in good faith and enter into a commercial supply agreement.

Individual patents extend for varying time periods depending on the effective date of filing the patent application or the date of patent issuance, and the legal term of the patents in the countries in which they are obtained. Generally, patents issued in the US are effective for the longer of 17 years from the issue date or 20 years from the earliest effective filing date, if the patent application 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 term of our foreign patents varies in accordance with provisions of applicable local law, but typically is 20 years from the earliest effective filing date.

License and Collaboration Agreements

License Agreements and Other Collaboration Agreements Relating to ARIKACE

PARI Pharma GmbH - We currently have a licensing agreement with PARI for use of the optimized eFlow Nebulizer System for delivery of ARIKACE in treating patients with CF, bronchiectasis, and NTM infections. Under the licensing agreement, we have rights to several US and foreign issued patents, and patent applications involving improvements to the optimized eFlow Nebulizer System. We currently have rights to use the nebulizers in clinical trials and PARI has agreed to negotiate in good faith and enter into a commercial supply agreement.

We are obligated under this licensing agreement to use commercially reasonable efforts to develop, commercialize, market, and sell ARIKACE for use in CF indications in one or more countries (and at least in the US). 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 ARIKACE and the device, first receipt of marketing approval in the US for ARIKACE and the device, and first receipt of marketing approval in a major EU country for ARIKACE and the device, and NDA acceptance and regulatory approval of ARIKACE. In addition, PARI is entitled to receive royalty payments in the mid-single digits on the net commercial sales of ARIKACE 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 ARIKACE 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.

Cystic Fibrosis Foundation Therapeutics, Inc. - In 2005 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 ARIKACE. If ARIKACE 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 sales milestones are met within 5 years of the drug commercialization approval in the US, we would owe an additional payment of $3.9 million.

National Institutes of Allergy and Infectious Diseases - In 2012, we entered into a cooperative research and development agreement (CRADA) with National Institutes of Allergy and Infectious Diseases (NIAID) to evaluate the safety and efficacy of ARIKACE in patients with NTM lung disease in our phase 2 clinical study. NIAID agreed to provide biostatistical advisory input in connection with the phase 2 NTM study. If we decide not to continue with the commercialization of ARIKACE in NTM, NIAID will have the right to complete the clinical trial. Further NIAID may elect to pursue its rights to obtain license rights to certain inventions made under the CRADA.

License Agreements and Other Collaboration Agreements Relating to Other Compounds

Ipsen and Genentech - In March 2007, 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. In November 2008 we gained Royalty-Free Worldwide Rights for IPLEX from Ipsen and Genentech in connection with potential expanded access ALS programs.

NAPO Pharmaceuticals - In January 2007, we entered into an agreement with NAPO Pharmaceuticals, whereby we granted NAPO a license for INSM-18 also known as Masoprocal. The license gives NAPO the right to develop, manufacture and commercialize Masoprocal products for any indications relating specifically to diabetes, cardiac disease, vascular disease, metabolic disease and Syndrome X. The agreement calls for payments from NAPO to us upon the achievement of certain milestones which have not yet been met.

TriAct - In December 2010, we entered into an agreement with TriAct Therapeutics Inc. ("TriAct") whereby we granted TriAct an exclusive license for INS-18 also known as Masoprocal. The license gives TriAct the right to develop, manufacture and commercialize Masoprocal products for any indications relating specifically to oncology. The agreement calls for the issue of TriAct common stock to Insmed upon the achievement of certain milestones. To date, no milestones have been achieved and no common stock has been received.

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 are 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, exercisable by Premacure any time prior to April 30, 2013, to pay us $11.5 million and assume any of our royalty obligations to other parties in exchange for a fully paid license. If Premacure exercises this option, we would not be entitled to future royalties from Premacure.

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, ARIKACE, 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 December 2012, we learned that the EMA had no objection to our use of the name ARIKACE. In early 2013, we learned that the FDA objected to our use of the name ARIKACE as our proposed trade name for our liposomal amakacin for inhalation product candidate. We have not decided whether to appeal the FDA's decision. Even if we do appeal we may be required to adopt an alternative name for our 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.

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 payors 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.

Major Competitors

Our major competitors include pharmaceutical and biotechnology companies that have approved therapies or therapies in development for the treatment of chronic lung infections. Most of these competitors are focused on the CF market for their lead indication. Inhaled antibiotics are a standard of care in the treatment of CF to manage the chronic *Pseudomonas* infections due to the high concentrations of drug deposited directly into the lung, where the infection resides.

Novartis has two products for the treatment of *Pseudomonas* lung infections in CF patients. Tobi was the first inhaled antibiotic to be approved by the FDA for the treatment of CF patients with *Pseudomonas* lung infections and has been sold in the US since January 1998. Tobi requires administration twice daily for approximately 15 to 20 minutes per treatment for a daily total of approximately 30 to 40 minutes per day. Tobi continues to be the most used product in Europe and the US. Tobramycin inhalation powder, also known as TIP or Tobi Podhaler ®, is a dry powder version of tobramycin approved by the EU in 2011 for use by CF patients with *Pseudomonas* . Novartis filed for approval of Tobi Podhaler in the US and the FDA is reviewing the application.

Forest Laboratories markets inhaled colistin in Europe under the name Colomycin ® as inhaled solution and Colobreathe as inhaled dry powder. Colistin is used in Europe primarily as an adjunct therapy and in some cases as a primary therapy. Because it is less expensive than Tobi, colistin is used as a first line treatment in some countries that have a more restrictive reimbursement system. Colistin is not approved for inhaled treatment in the US, but it is frequently used off label (via pharmacist compounding) for patients that cannot use Tobi and for more severe patients in the off month alternating with Tobi in an attempt to maintain lung function in patients who are deteriorating on Tobi alone.

Gilead Sciences markets Cayston ® (aztreonam for inhalation) which received approval from the FDA in early 2010. Cayston requires administration three times per day for two to three minutes for each treatment for a daily total of approximately about 10 minutes. Gilead received conditional approval for Cayston in Europe during September 2009. Cayston is approved for one cycle of treatment.

In addition, we are aware of at least two other companies, Aptalis Pharmaceuticals and KaloBios Pharmaceuticals, which have products potentially competitive to ARIKACE currently in development.

Market data on marketed competitors for the treatment of *Pseudomonas* lung infections in CF patients as reported by the individual companies is summarized below.

Competitor	Product/Product Candidate for *Pseudomonas* Lung Infections in CF Patients	Class of Product	Key Marketing Approvals	2012 Reported Sales (millions)
Novartis	Tobi (Tobramycin Inhalation Solution or TIS)	Aminoglycoside	Europe, US and Canada	$ 276
Novartis	Tobi Podhaler (Tobramycin Inhalation Powder or TIP)	Aminoglycoside	Europe and Canada; application filed in US	$ 41
Gilead	Cayston (Aztreonam for Inhalation Solution)	Monobactam	Europe and US	$ 107
Forest	Colimycin (Colistimethate Sodium for Inhalation)	Polymixin	Europe	Not reported
Forest	Colobreathe (Colistimethate Sodium Powder)	Polymixin	Europe	Not reported
Chiesi	Bramitob ® (Tobramycin Inhalation Solution)	Aminoglycoside	Europe	Not reported
Aptalis Pharmaceuticals	Aeroquin ™ (Inhaled Levofloxacin)	Flouroquinolone	None - Phase 3 (data reported)	Not approved
KaloBios Pharmaceuticals	KB001-A (IV administered PEGylated mAb fragment)	Monoclonal Antibody	None - Phase 2 (initiated January 2013)	Not approved

We are not aware of any other companies developing an inhaled antibiotic for NTM lung infections. While there is no approved treatment for NTM lung infections, there is an American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) treatment regimen that is utilized.

GOVERNMENT REGULATION

Orphan Drugs

European Union

The EMA grants orphan drug designation to promote the development of products that may offer therapeutic benefits for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the EU. In addition, orphan drug designation can be granted if the drug is intended for a life threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that sales of the drug in the EU would be sufficient to justify developing the drug. Orphan drug designation is available either if there is no other satisfactory method approved in the EU of diagnosing, preventing or treating the condition or if a method does exist, but the proposed orphan drug will be of significant benefit to patients.

Orphan drug designation provides opportunities for free protocol assistance and fee reductions for access to the centralized regulatory procedures before and during the first year after marketing approval, which reductions are not limited to the first year after marketing approval for small and medium enterprises. In addition, if a product which has an orphan drug designation subsequently receives EMA marketing approval for the indication for which it has such designation, the product is entitled to orphan drug exclusivity, which means the EMA may not approve any other application to market the same drug for the same indication for a period of ten years. The exclusivity period may be reduced to six years if the designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Competitors may receive marketing approval of different drugs or biologics for the indications for which the orphan product has exclusivity. In order to do so, however, they must demonstrate that the new drugs or biologics provide a significant benefit over the existing orphan product. This demonstration of significant benefit may be done at the time of initial approval or in post-approval studies, depending on the type of marketing authorization granted.

United States

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the US. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation provides certain exclusivity benefits, tax credits for certain research and a waiver of the NDA application user fee. However, it does not convey any advantage in or shorten the duration of the regulatory review and approval process. The first NDA applicant with FDA orphan drug designation for a particular active ingredient to receive FDA approval of the designated drug for the indication for which it has such designation, is entitled to a seven-year exclusive marketing period, often referred to as orphan drug exclusivity, in the US for that product 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.

Drug Approval

Europe

To obtain approval of a drug under EU regulatory systems, we may submit marketing authorizations either under a centralized or decentralized procedure. These procedures apply in the EU member states, plus the European Economic Area countries, Norway and Iceland. The centralized procedure, which is compulsory for medicines produced by certain biotechnological processes and for orphan drugs and is optional for those which are highly innovative, provides for the grant of a single marketing authorization that is valid for all EU member states. Under this procedure, an applicant submits an application, including a summary of product characteristics and proposed labeling and packaging, to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state’s assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to the public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

United States

In the US, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act 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 may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve and even accept for review pending new drug applications, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

Pharmaceutical product development in the US typically involves non-clinical laboratory and animal tests, the submission to the FDA of a notice of claimed investigational exemption or an investigational new drug (IND) application, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. 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 tests include laboratory evaluation of product chemistry, formulation and toxicity, 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 good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information including information about product chemistry, manufacturing and controls and a proposed clinical trial protocol. Certain non-clinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may be performed after the IND is submitted.

A 30-day waiting period after the submission of an IND is required prior to the commencement of clinical testing in humans. If the FDA has not placed the proposed clinical trial on hold within this 30-day period and the applicable institutional review board(s) has approved the trial, the clinical trial proposed in the IND may begin.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose 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 patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. 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 phases, but the phases may overlap. For phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication or indications, dosage tolerance and optimum dosage and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in phase 2 evaluations, phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug.

After completion of the required clinical testing, a NDA is 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 the manufacturer and/or sponsor under an approved new drug application are also subject to annual product and establishment user fees. 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 an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for non-priority drug products are reviewed within twelve months of submission. The review process may be extended by FDA for three additional months to consider certain information or clarification regarding information already provided in the submission.

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 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 an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with Good Clinical Practice. Additionally, the FDA will 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 studied.

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 such resubmissions in two or six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require 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. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Upon NDA approval, the approved drug receives five years of marketing exclusivity during which FDA cannot receive any ANDA seeking approval of a generic version of that drug except under certain circumstances. Certain changes to a drug, such as the addition of a new indication to the package insert, are associated with a three-year period of exclusivity during which FDA cannot approve an ANDA for a generic drug that includes the change. After NDA approval, owners of relevant drug patents may apply for up to a five-year patent extension. 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 an NDA has not been submitted.

Fast Track Designation

Under the fast track program, 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.

In addition to other benefits such as the ability to have more interactions with FDA, FDA may initiate review of sections of a fast track drug's NDA before the application is complete. This rolling review is available if the applicant provides and FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, the fast track designation may be withdrawn by FDA if FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Priority Review

Under FDA policies, a drug candidate is eligible for priority review, or review within an eight-month time frame from the time an NDA is submitted, if the drug candidate provides a significant improvement compared to marketed drugs in the treatment, diagnosis or prevention of a disease. A fast track designated drug candidate would ordinarily meet FDA's criteria for priority review. The FDA makes its determination of priority or standard review during the 60-day filing period after a NDA submission.

Combination Products

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

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

Antibiotic Exclusivity

A drug product designated by the FDA as a qualified infectious disease product, or QIDP, is granted an additional five years of marketing exclusivity upon NDA approval. This exclusivity applies only with respect to drugs that are first approved on or after July 9, 2012. A QIDP is defined as an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens or certain pathogens that have the potential to pose a serious threat to public health and that are included in a list established and maintained by 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. Any NDA for a drug designated as a QIDP will be granted priority review.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, study sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss 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 Regulatory Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet.

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, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can 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.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, risk minimization action plans and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product.

In addition, quality control as well as drug manufacture, packaging, and labeling procedures must continue to 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. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMPs.

Regulatory authorities may withdraw product approvals or request product recalls if a Company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Pediatric Information

European Union

For the EMA, pediatric data or an approved pediatric investigation plan, or PIP, is required to submit an MAA in the European Union. In December 2010, we received Positive Opinion of the Pediatric Committee of the EMA on the agreement of our PIP, on the granting of a deferral, and on the granting of a waiver for amikacin (sulfate) nebulizer suspension for inhalation use, in the treatment of *Pseudomonas* lung infection/colonization in CF patients in accordance with relevant European regulations. Our PIP is subject to modifications from time to time.

United States

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant 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 negotiate the terms of the 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).

Medical Device Regulation

If approved, ARIKACE will be administered via inhalation through an optimized eFlow Nebulizer System, which is a medical device that is also subject to extensive government regulation. The optimized eFlow Nebulizer System is approved in the EU, and it must be approved in any country in which we intend to commercialize ARIKACE.

Similar to an NDA-approved product, the medical device is subjected to certain post-clearance requirements. Those requirements include continuing Quality System compliance, Medical Device Reporting, and promotional material regulations.

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 with ARIKACE, 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. CE mark is standard designation for EU member States for market authorization.

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 federal program administered by the states to provide health care benefits to certain indigent persons. In return for including our pharmaceutical commercial products in the Medicare and Medicaid programs, 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 programs 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.

Different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products 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 consumers. Some jurisdictions operate positive and negative list systems under which products 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 medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. 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 dug products will allow favorable reimbursement and pricing arrangements for any of our products.

EMPLOYEES

As of December 31, 2012, we had a total of 41 employees, including 18 in research, clinical, regulatory and quality assurance; 11 in technical operations, manufacturing and quality control; and 12 in general and administrative functions. We anticipate additional hires in 2013.

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, ARIKACE. If we are unable to successfully complete the development of, obtain regulatory approval for, and commercialize ARIKACE, 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 ARIKACE, our most advanced product candidate. Our ability to generate product revenue from ARIKACE, which we do not expect will occur for at least the next several years, if ever, will depend heavily on the successful completion of development of, receipt of regulatory approval for and commercialization of ARIKACE.

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 ARIKACE may not be predictive of the results we may obtain in our clinical trials currently in progress or other trials. We do not expect ARIKACE or any other drug candidates we may develop to be commercially available for at least several years, if at all.

We have not completed the research and development stage of ARIKACE or any other product candidates other than IPLEX, which we no longer market. If we are unable to successfully commercialize ARIKACE 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 ARIKACE 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 FDA disease-specific expectations;
- 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; 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 ARIKACE program in the CF or NTM 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 ARIKACE, we may not obtain labeling that permits us to market them with commercially viable claims because our clinical trials may not provide head-to-head comparisons with other drugs. Failure to successfully commercialize our products will adversely affect our business, financial condition, results of operations and prospects.

If the FDA or EMA limits our proposed CF or NTM treatment population for ARIKACE, our preclinical 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. We initiated a phase 2 NTM study in the US, fully enrolled patients in a phase 3 trial for CF patients with *Pseudomonas* lung infection in Europe and Canada, and initiated a two-year CF extension study in Europe and Canada. In addition, as discussed below, in 2011 the FDA requested that we conduct a 9-month dog inhalation toxicity study to determine if the findings of the long-term rat inhalation carcinogenicity study with ARIKACE are observed in a non-rodent model.

Preclinical and clinical testing is expensive, difficult to design and implement and can take many years to complete. 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 program;
- 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, or clinical investigators 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.

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.

For example, results from our rodent carcinogenicity study showed that when rats were given ARIKACE daily by inhalation for two years, 2 of the 120 rats receiving the highest dose had a single lung tumor. These rats received ARIKACE 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 ARIKACE, which holds were lifted in 2012. While we are conducting a dog toxicology study to better understand the impact of ARIKACE on another animal model to satisfy the FDA's request, approvability or labeling of ARIKACE may be negatively affected by these results. In late January 2013, we concluded the 9 month dosing phase of the dog inhalation toxicity study. Consistent with the design of the study, a review of the lung and kidney tissues was conducted following the completion of the 9 month dosing and an unaudited interim report was prepared setting forth the findings of this review. We recently submitted this unaudited interim report to the FDA While we await final results from ongoing studies and trials, we do not know whether we will proceed with our clinical program for ARIKACE for the treatment of *Pseudomonas* lung infections in CF patients in the US. In addition, we do not know whether any additional preclinical tests, other than the dog inhalation toxicity study or clinical trials, will be required or otherwise initiated, will need to be restructured or will be completed on schedule, if at all. 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. Our product development costs have and may continue to increase if we experience further delays in testing or approvals.

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. ARIKACE and the nebulizer each are supplied by a sole manufacturer. We are dependent on Althea Technologies for the production of ARIKACE. We are dependent upon PARI for the production and supply of the eFlow Nebulizer System. 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 future operating results.

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 ARIKACE receives marketing approval. 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 are dependent upon Althea being able to provide an adequate supply of ARIKACE both for our clinical trials and for commercial sale in the event ARIKACE receives marketing approval. Althea currently manufactures ARIKACE at a relatively small scale. In order to meet potential commercial demand if ARIKACE is approved, we will need to work with Althea and others to increase the scale of our manufacturing activities. We intend to work closely with Althea to coordinate efforts regarding regulatory requirements and our supply needs.

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 foreign 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. Commercial manufacturing and supply agreements have not been established. 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.

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 phase 3 clinical trial 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. We have limited experience in conducting and managing the application process necessary to obtain regulatory approvals 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 ARIKACE, 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 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' clinical studies for the same patient population; and
- Ability to obtain any necessary comparator drug or medical device.

We believe our procedures for enrolling patients to date have been appropriate. However, delays in patient enrollment would increase costs and delay ultimate commercialization and sales, if any, of our products.

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

Even if we are able to successfully complete development of, obtain regulatory approval for, and bring ARIKACE to market, ARIKACE may not gain market acceptance by physicians, patients, third-party payors and others in the medical community. If ARIKACE 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 ARIKACE 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 or 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 payors 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 no 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 do not have a sales organization for the marketing, sales and distribution of any drug products. In order to commercialize ARIKACE 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. 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 ARIKACE. However, we may not be able to enter into arrangements with third parties to sell ARIKACE on favorable terms or at all. In the event we are unable to develop our own marketing and sales force or collaborate with a third-party marketing and sales organization, we may not be able to successfully commercialize ARIKACE 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.

Risks Related to Our Reliance on Third Parties

We rely on third parties including clinical research organizations, or CROs, 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 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. 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;
- 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 exclusively used for ARIKACE. 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 ARIKACE receives marketing approval. These nebulizers must be in good working order, meet specific performance characteristics and be approved by FDA along with ARIKACE. We have no alternative supplier for the nebulizer and we do not intend to seek an alternative or secondary supplier of nebulizers. We do not have a long-term supply agreement with PARI. PARI 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, 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, including the requirement that we use commercially reasonable efforts to develop, commercialize, market, and sell ARIKACE for use in CF indications in one or more countries (and at least in the US). 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 Althea, a third party manufacturer, to supply ARIKACE. Any disruption in the supply of ARIKACE could have a material adverse effect on our business.

We are dependent upon Althea being able to provide an adequate supply of ARIKACE both for our clinical trials and for commercial sale in the event ARIKACE receives marketing approval. Althea currently manufactures ARIKACE at a relatively small scale. In order to meet potential commercial demand if ARIKACE is approved, we will need to work with Althea to increase the scale of our manufacturing activities. We do not have a long term supply agreement with Althea. Althea recently announced that it had entered into an agreement to be acquired by Ajinomoto Co., a global manufacturing company based in Japan. We do not know at this point how this contemplated acquisition might affect our relationship with Althea, if at all.

We intend to identify other third parties to manufacture ARIKACE. We also intend to have ARIKACE manufactured at a larger scale in order to meet potential demand if ARIKACE is approved for sale. We may not be able to identify or secure an alternative source of ARIKCACE at an adequate scale of production.

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

We rely on third parties, such as CROs, 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 ARIKACE 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.

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 biopharmaceutical company focused on the development of innovative inhaled pharmaceuticals for the site-specific treatment of serious lung 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 establish a sales and marketing organization and 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, 2012, our accumulated deficit was $335.5 million. For the year ended December 31, 2012, our consolidated net loss was $41.4 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 ARIKACE and possibly other product candidates which have yet to be developed and which would also require marketing approval;
- Commercializing ARIKACE and any other product candidates for which we obtain marketing approval; and
- Achieving market acceptance and reimbursement of ARIKACE and any other product candidates for which we obtain marketing approval in the medical community and with patients and third-party payors.

ARIKACE 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 ARIKACE 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 ARIKACE. We may need to seek additional funding in order to complete any clinical trials related to ARIKACE, seek regulatory approvals of ARIKACE, and commercially launch ARIKACE. We also may require additional future capital in order to continue our other research and development activities or to acquire complementary technology. As of December 31, 2012, we had $92.9 million of cash and cash equivalents and a certificate of deposit 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 2 and phase 3 clinical trials and commercialization of ARIKACE;
- Non-clinical and clinical testing;
- Process development and scale up for manufacturing;
- Manufacturing;
- 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;
- Filing and prosecuting patent applications and enforcing patent claims;
- Establishing strategic alliances and collaborations with third-parties; and
- Current 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, 2012, 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.

We generated no revenue in 2012. Our revenue from our expanded access program, or EAP, and the sale of IPLEX were our only material sources of operating revenue prior to 2012. Unless we can execute one or more revenue generating transactions or successfully obtain regulatory approval for and commercialize ARIKACE, 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 ARIKACE.

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.

We continue to evaluate possible out-licensing opportunities for IPLEX. We may have difficulty identifying possible markets and prospective partners for out-licensing. 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). In conjunction with entering into the Loan Agreement, we granted a warrant to the lender to purchase 329,932 shares of our common stock for $2.94 per share. 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 over 37% of our total assets. A reduction in the value of our IPRD could impact our results of operations.

As a result of the merger with Transave we recorded an intangible IPRD asset of $77.9 million and goodwill of $6.9 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.

We may be unable to use our net operating losses.

We have substantial tax loss carry forwards for US federal income tax purposes. Our ability to use such carry forwards to offset future income or tax liability may be 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 warrants or options, may limit or eliminate our ability to use our net operating losses.

Risks Related to Regulatory Matters

We may not be able to obtain regulatory approvals for ARIKACE 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.

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.

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.

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

Although the optimized eFlow Nebulizer System is CE marked by PARI outside of North America, within North America it is labeled as investigational for use in our clinical trials in the US and Canada. 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 ARIKACE if approved. The eFlow Nebulizer System must receive regulatory approval before we can market ARIKACE. We will continue to work closely with PARI to coordinate efforts regarding regulatory requirements, including our proposed filings for a drug and device.

Even if we obtain marketing approval for ARIKACE 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, 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 ARIKACE 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 ARIKACE 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;
- 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;
- 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 candidate, 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 payors for ARIKACE 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 payors, both in the US and in other markets. Reimbursement by a third party payor may depend upon a number of factors, including the third party payor's determination that use of a product is:

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

Obtaining reimbursement approval for a product from each government or other third-party payor 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 payor. 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 payors' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Even when a payor determines that a product is eligible for reimbursement, the payor 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. We expect changes in the Medicare program and state Medicaid programs, as well as managed care organizations and other third-party payors to continue to put pressure on pharmaceutical product pricing. 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 coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for drugs. In addition, this legislation authorized Medicare Part D prescription drug plans to use formularies where they can limit the number of drugs that will be covered in any therapeutic class. As a result of this legislation and the expansion of federal coverage of drug products, we expect that there will be additional pressure to contain and reduce costs. These cost reduction initiatives and other provisions of this legislation 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 payors 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 payors.

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 new 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. Although it is too early to determine the effect of the PPACA, 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 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 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 PPACA, which may require us to modify our business practices with health care practitioners. For example, beginning in 2013, drug manufacturers will be required to report information on payments or transfers of value to physicians and teaching hospitals as well as investment interests held by physicians and their immediate family members during the preceding calendar year. Failure to submit required information may result in civil monetary penalties. Although the statute requires reporting by March 31, 2013 of payments and other transfers of value made in calendar year 2012, the Centers for Medicare & Medicaid Services, or CMS has issued a final rule that will go into effect in April 2013 and will require manufacturers to begin collecting required information on August 1, 2013, with the first reports due March 31, 2014. The reported data will be posted in searchable form on a public website beginning September 30, 2014.

The reforms imposed by the new law will significantly impact the pharmaceutical industry; however, the full effects cannot be known until these provisions are implemented and CMS and other federal and state agencies 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 objected to our use of the name ARIKACE as our proposed trade name for our liposomal amakacin for inhalation product candidate. We have not decided whether to appeal the FDA's decision. Even if we do appeal we may be required to adopt an alternative name for our product candidate. Until the FDA approves a trade name or 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 ARIKACE could be delayed or interrupted, which would limit our ability to commercialize ARIKACE and generate revenues. In December 2012, we learned that the EMA had no objection to our request to use the names ARIKACE.

Our growth depends on technologies that may not be available on terms acceptable to us or at all.

As part of our business strategy, we may in-license new products and technologies. Nonetheless, we cannot assure you that we will identify suitable products or enter into such license agreements on acceptable terms.

We 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.

Certain of our collaborators could be or become competitors of ours. Our collaborators could harm our product development and commercialization efforts by:

- Developing competing products;
- Precluding us from entering into collaborations with their competitors;
- Failing to obtain regulatory approvals;
- Terminating their agreements with us prematurely; or
- Failing to devote sufficient resources to the development and commercialization of products.

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 United States, 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 payors, including government payors, 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 resulted in the submission of false claims to governmental health care programs. 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 payors, 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 U.S. 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 payors. 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. 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.

Changes in either patent laws or in interpretations of patent laws in the US 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 US 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-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, currently 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 how the FDA’s disclosure policies may change in the future, if at all. 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.

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 issued patents, or patents that may later issue to third parties, would not negatively affect our commercialization of ARIKACE 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:

- 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; or
- Obtain one or more licenses arising out of a settlement of litigation or otherwise from third parties for the infringed proprietary rights, which 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.

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 validate 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 exclusive use of the optimized eFlow Nebulizer System for delivery of ARIKACE in treating patients with CF, bronchiectasis and 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 ARIKACE and the device, first receipt of marketing approval in the US for ARIKACE and the device, and first receipt of marketing approval in a major EU country for ARIKACE and the device. We are required to use commercially reasonable efforts to pursue the clinical development of ARIKACE in one or more countries and, for CF at least in the United States, and after obtaining such marketing approval to use commercially reasonable efforts to market and sell ARIKACE in the countries in which it is approved. If we fail to meet some or all of our obligations under the licensing agreement or choose to discontinue commercialization of ARIKACE in any indication, PARI may compete in the indication, we may lose the exclusive rights to use the PARI device with ARIKACE in the indication, and we may lose the non-exclusive right to use the PARI device with ARIKACE in the 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 ARIKACE. PARI may also choose to terminate the agreement if we do not use commercially reasonable efforts over a two year period of time.

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 large 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.

If ARIKACE is approved for *Pseudomonas* lung infections in CF patients, it will compete against Tobi, the current standard of care for the chronic management of these infections. Tobi is marketed by Novartis. Other competitors in this market include Gilead and Forest, and we are aware of other companies also developing products for this indication. We cannot assure you that if ARIKACE is approved for this indication or NTM that it will be able to compete successfully in the marketplace.

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

In the event there are other amikacin products approved by the FDA for any use, physicians may elect to prescribe those products rather than ARIKACE to treat the indications for which ARIKACE may receive approval, which is commonly referred to as off-label use. Although FDA regulations prohibit a drug company from promoting off-label use of its product, the FDA does 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 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 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 ARIKACE-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 due to *Pseudomonas.* If any of our competitors develops a product that is more effective, safer, tolerable or, convenient or less expensive than ARIKACE, it would adversely affect our ability to generate revenues. We also may face lower priced generic competitors if third-party payors encourage use or generic or lower-priced versions of our product or if competing products are imported into the US from Canada, Mexico or other countries.

FDA approval of products that treat the underlying cause of CF could reduce the market opportunity for ARIKACE.

In January 2012, the FDA approved Kalydeco (ivacaftor) by Vertex as the first drug approved to treat patients with the G551D mutation of CF, which affects about 4% of CF patients. Vertex also is studying Kalydeco, in combination with another drug candidate, for a more common CF mutation. We cannot predict the potential effects of Kalydeco or similar products approved in the future on inhaled antibiotic use in CF. It is possible that these therapies could decrease the number or proportion of CF patients who acquire *Pseudomonas* lung infections and thereby decrease the market for inhaled antibiotics like ARIKACE.

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, which is generally a disease or condition that affects fewer than 200,000 individuals in the US. 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, as ARIKACE was for treating CF patients with *Pseudomonas* , 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.

Our research, development and manufacturing activities used in the production of ARIKACE 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, development and manufacturing activities for ARIKACE involve the controlled use of hazardous materials and chemicals. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In addition to any liability we could have for any use 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 ARIKACE.

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.

As described under "—If we fail to meet the continued listing requirements of the Nasdaq Capital Market, our common stock may be delisted from Nasdaq and the value of our common stock may decrease," we made equity awards to key personnel and directors and portions of certain of these equity awards were deemed to be in excess of our 2000 Stock Incentive Plan per person sub-limits. We are requesting that our shareholders approve, at our 2013 annual meeting of shareholders, the excess portions of certain equity awards. If our shareholders do not ratify and approve the affected portions of such awards, our current affected officers and directors agreed that such portions would be deemed forfeited. Such forfeiture could make it difficult for us to retain the services of the affected key personnel, particularly if we are otherwise unable to provide them with equity compensation that is competitive with the market place. In addition, such forfeitures may reduce the morale of the affected recipients and may cause a more widespread reduction in employee morale, which could make it more difficult for us to retain qualified employees and to hire qualified employees in the future. Our inability to retain and attract qualified employees would harm our business.

We expect to expand our development, 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 ARIKACE 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 Capital Market

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

Our common stock is listed on the Nasdaq Capital 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 Capital 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, shareholder 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.

At the time of our merger with Transave, certain former Transave stockholders holding approximately 40% of our shares of common stock as of December 1, 2010, entered into lock-up arrangements with us in connection with the merger. The lock-up arrangements expired on May 30, 2012, and these shareholders may now generally dispose of all their shares freely except to the extent that any such shareholder is an affiliate of the Company. Such Transave stockholders have the benefit of a registration rights agreement dated December 1, 2010, pursuant to which the Transave stockholders may, subject to certain conditions, require us to file registration statements covering the resale of their shares of common stock or to include their shares of common stock in registration statements that we may file for ourselves or other stockholders. We have also granted certain registration rights to Hercules in respect of the warrant issued to them in connection with our Loan Agreement.

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

As a result of the events described below or for other reasons not currently known to us, Nasdaq may determine that we have not met the continued listing requirements of the Nasdaq Capital Market. If a delisting from the Nasdaq Capital 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 Capital Market. Therefore, delisting of our common stock from the Nasdaq Capital 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.

On October 12, 2012, the Nasdaq staff issued a Letter of Reprimand to us pursuant to Nasdaq Listing Rule 5810(c)(4), based on its noncompliance with Nasdaq Listing Rule 5635(d). The Letter of Reprimand related to the registered direct financing we closed on September 28, 2012. In that financing, we issued 6,304,102 shares of common stock to three investors. The price at which the common stock was sold in the financing was $4.07 per share, equal to the closing bid price for our common shares on the day prior to the issuance. On October 5, 2012, we received telephonic notice from our outside counsel on the transaction that the Nasdaq staff had informed such counsel of the staff's belief that the sale of the shares did not comply with Nasdaq Listing Rule 5365(d). The staff's concern was based on the fact that the shares were sold at a price that was below the book value per share of our stock as reflected in our Form 10-Q for the quarter ended June 30, 2012. As a result, it was the staff's belief that, pursuant to the Nasdaq Listing Rules, we were not permitted to issue 20% or more of our outstanding common shares in the financing, even though the sales price per share was equal to the market value per share on the date immediately preceding the issuance. The Staff previously informed us that, having issued the Letter of Reprimand to us, it considered the matter closed.

In connection with a recent review by us of equity compensation awards made by us under our Amended and Restated 2000 Stock Incentive Plan, as amended (the "2000 Stock Incentive Plan"), pursuant to which we may grant stock-based awards to our employees, executive officers, directors and certain of our advisors and service providers, we determined that we had inadvertently exceeded the annual per-person sub-limits set forth in the 2000 Stock Incentive Plan in connection with awards previously made to certain of our current and past officers and directors. The aggregate amount of common stock represented by these awards in excess of the per person annual sub-limits, which consisted of restricted stock, RSUs and stock options, is approximately 1.6 million shares. The awards that we determined exceeded the per person sub-limits included certain awards issued immediately following our business combination with Transave, awards negotiated with new hires pursuant to employment agreements or offers of employment, and certain other awards made subsequent to our 2011 one-for-ten reverse stock split. We have not exceeded the aggregate maximum share limit approved by shareholders under the 2000 Stock Incentive Plan (currently 3,925,000 shares of common stock), whether as a result of previously-issued awards or currently outstanding awards.

On March 12, 2013, we notified Nasdaq of the grants previously made in excess of the annual per-person sub-limits provided for by the 2000 Stock Incentive Plan. We believe that a decision by us to increase the annual sub-limits would have constituted an immaterial amendment to the 2000 Stock Incentive Plan, which amendment would not have required shareholder approval under applicable Nasdaq guidance. However, because the grant of certain awards exceeded the sub-limits applicable at the time the grants were made, it is possible that Nasdaq will conclude that we issued securities pursuant to the 2000 Stock Incentive Plan without shareholder approval in violation of Nasdaq Listing Rule 5635(c).

In a March 13, 2013 letter to Nasdaq, we submitted a remediation and compliance plan, which we refer to as our remediation plan, to address the grants made in excess of the 2000 Stock Incentive Plan sub-limits. Among other items, our remediation plan conditions the continued vesting and exercise of the portion of each equity compensation award issued to our current employees and directors in excess of the 2000 Stock Incentive Plan's sub-limits on approval by our shareholders of such portion of the affected grants. If our shareholders do not ratify and approve the affected portions of such awards, such portions would be deemed forfeited.

We cannot assure you that Nasdaq will not determine to delist us or issue us another reprimand letter in connection with our grants of equity awards to certain employees and directors in excess of the annual per-person sub-limits provided for in our 2000 Stock Incentive Plan. If either of these things were to occur, it could have a material adverse effect on the trading price and liquidity of our common stock.

The ownership interest of existing shareholders will be diluted by the exercise of warrants and 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 February 28, 2013, warrants issued by us in June 2012 to Hercules were exercisable at a price of $2.94 per share for up to approximately 329,932 shares of our common stock. Such warrants expire on June 29, 2017.

As of February 28, 2013, 2,180,310 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 warrants, 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 February 28, 2013 we had 31,563,278 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

On January 30, 2013, our Board received a letter purportedly on behalf of one of our shareholders who made a demand on the Board to investigate and take appropriate remedial measures in relation to our 2012 grant of stock options to Mr. Will Lewis, our President and Chief Executive Officer. If this purported shareholder initiates litigation against us, or if we become subject to other litigation or legal proceedings in connection with our grants of stock options in excess of our 2000 Stock Incentive Plan sub-limits, we could be required to expend significant resources in connection with defending any such litigation or other legal proceedings, and any unfavorable outcome in any such litigation or other legal proceedings could materially adversely affect our business, financial condition or results of operations.

On January 30, 2013, our Board received a letter purportedly on behalf of one of our shareholders who made a demand on the Board to rescind certain stock options granted to our President and CEO, Mr. Lewis, in excess of our 2000 Stock Incentive Plan sub-limits and to adopt and implement adequate internal controls designed to prevent future issuances in excess of our 2000 Stock Incentive Plan sub-limits. Upon receipt of the demand letter, our Board formed a special committee of independent directors, which we refer to as the Special Committee, to investigate the allegations in the letter and, if necessary, to recommend necessary and appropriate remediation measures. The Special Committee retained counsel to assist it in its investigation. The Special Committee determined that we had inadvertently exceeded the 2000 Stock Incentive Plan's annual per-person sub-limit applicable to the stock options granted to Mr. Lewis. Separately, on its own initiative, the Special Committee investigated grants that were not addressed in the demand letter, and it determined that we had inadvertently granted certain other equity awards that exceeded annual per-person sub-limits. Following its investigation, the Special Committee made recommendations to our Board. On March 7, 2013, our Board approved a remediation and compliance plan that provides for various remediation measures, including securing the waiver and consent agreements entered into by our current affected employees and directors, as well as obtaining shareholder approval of the affected portion of certain equity awards granted under the 2000 Stock Incentive Plan.

We cannot assure you that the purported shareholder who sent the demand letter, or our other shareholders or other parties, will not initiate litigation or other legal proceedings, despite our remediation efforts relating to the option grants to Mr. Lewis or the other issues relating to options described above. Litigation and other legal proceedings can be expensive, lengthy and disruptive to normal business operations. Moreover, the results of complex legal proceedings are difficult to predict. Responding to lawsuits or other legal proceedings brought against us or our Board could be expensive and time-consuming. Unfavorable outcomes from these claims or lawsuits or other legal proceedings could materially adversely affect our business financial condition or results of operations, and we could incur substantial monetary liability or be required to change our business practices, among other remedies that might be imposed.

We have identified a material weakness in our internal control over the administration, accounting and oversight of our 2000 Stock Incentive Plan, and our business and stock price may be materially adversely affected if we do not adequately address this material weakness or if we have other material weaknesses or significant deficiencies in our internal control over financial reporting.

As a public company, we are required, pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. 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 have therefore 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. Until we have been able to test the operating effectiveness of remediated internal controls and ensure the effectiveness of our disclosure controls and procedures, 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 additional weaknesses in our internal control over financial reporting. Any such additional weakness or failure to remediate the existing material weakness could materially adversely affect our ability to comply with applicable financial reporting requirements and the requirements of our various agreements. Further, if we cannot produce reliable financial reports, investors could lose confidence in our reported financial information, the market price of our stock could decline significantly, we may be unable to obtain additional financing to operate and expand our business, and our business, financial condition and results of operations could be materially harmed.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We currently lease a facility totaling 27,035 square feet of laboratory and office space at 9 Deer Park Drive in Monmouth Junction, New Jersey. The lease expires in December 2014. We also lease approximately 1,350 sq. ft. of lab space at 11 Deer Park Drive, which also expires in December 2014. The additional space at 11 Deer Park Drive is utilized to support the manufacturing process of ARIKACE for our clinical programs.

We also lease approximately 18,000 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 and are attempting to sublet this space.

ITEM 3. LEGAL PROCEEDINGS

Cacchillo v. Insmed

On October 6, 2010, a complaint was filed against us by Angeline Cacchillo ("Plaintiff") in the U.S. District Court for the Northern District of New York (the "Court"), captioned *Cacchillo v. Insmed, Inc.* , No. 1:10-cv-0199, seeking monetary damages and a court order requiring Insmed to support Plaintiff's compassionate use application to the FDA and if approved, to provide Plaintiff with IPLEX. Plaintiff was a participant in the phase II clinical trial of IPLEX sponsored by us evaluating the effectiveness of the investigational drug in patients with type 1 myotonic muscular dystrophy ("MMD"). In the complaint, Plaintiff alleged (i) violation of constitutional due process and equal protection by depriving Plaintiff of continued access to IPLEX, (ii) fraudulent inducement to enter the phase II clinical trial with the false promise to support Plaintiff's compassionate use application to the FDA, (iii) negligent representation that we would support Plaintiff's compassionate use application, (iv) breach of contract, seeking monetary and non-monetary damages, (v) intentional infliction of emotional distress by refusing to support Plaintiff's compassionate use application after providing IPLEX, (vi) violation of an assumed duty of care to Plaintiff, (vii) breach of fiduciary duty to Plaintiff, (viii) negligence and (ix) unjust enrichment. Plaintiff seeks compensatory and punitive monetary damages and sought injunction relief as noted above.

On October 7, 2010, Plaintiff filed a motion for a preliminary injunction that would require us to provide a written statement supporting the "compassionate use" of IPLEX for Plaintiff and directing us to provide IPLEX to Plaintiff at cost in the event that the compassionate use application were granted by the FDA. On October 22, 2010, the Court denied Plaintiff's motion for the preliminary injunction concluding that the Court lacked subject matter jurisdiction with respect to her claim for a preliminary injunction. Plaintiff appealed the Court's denial of her motion for a preliminary injunction to the U.S. Court of Appeals for the Second Circuit, which affirmed the trial court's order denying the Plaintiff's motion for a preliminary injunction.

We filed a motion with the Court to dismiss all of the outstanding claims, and on June 29, 2011, the Court dismissed six of Plaintiff's claims, leaving outstanding the claims for (i) fraudulent inducement, (ii) negligent misrepresentation, and (iii) breach of contract. We filed an answer and affirmative defenses with the Court on July 12, 2011. Plaintiff's claim for monetary damages with respect to these claims remains outstanding. The parties completed discovery on or about June 1, 2012. We filed a Motion for Summary Judgment on August 1, 2012 seeking judgment in our favor on the three claims remaining in the case and the motion was fully submitted on October 9, 2012. On January 19, 2013, the Court granted our Motion for Summary Judgment and dismissed all of the outstanding claims. Plaintiff filed a Notice of Appeal on March 15, 2013. We expect that the parties will submit briefs before the end of 2013, with a decision expected sometime in the first half of 2014.

Pilkiewicz v. Transave LLC

On March 28, 2011, Frank G. Pilkiewicz and other former stockholders of Transave (collectively, the "Petitioners") filed an appraisal action against our subsidiary Transave, LLC in the Delaware Court of Chancery captioned *Frank G. Pilkiewicz, et al. v. Transave, LLC* , C.A. No. 6319-CS. On December 13, 2011, following the mailing of the revised notice of appraisal rights in accordance with the settlement terms of *Mackinson et al. v. Insmed* , Petitioners filed an Amended Petition for Appraisal of Stock.

The Petitioners seek appraisal under Delaware law of their common stock holdings, representing approximately 7.77 million dissenting shares of Transave, Inc. common stock (the "Transave Stock"). The Petitioners have challenged the value of the consideration that they would be entitled to receive for their Transave Stock under the terms of the merger.

Under the terms of the merger agreement, certain of the former stockholders of Transave (the "Transave Stockholders") are obligated to indemnify us for certain liabilities in connection with the appraisal action. Certain indemnification and other obligations of the Transave Stockholders were secured by a holdback of 1.76 million shares of our common stock. In May 2012, we notified the Transave Stockholders that we are seeking indemnification from them and that we will continue to retain all 1.76 million holdback shares as security for any indemnification payments due to us. Discovery is ongoing and the trial is scheduled to begin September 30, 2013. We believe the allegations contained in the amended petition are without merit and we intend to continue to vigorously defend this action. It is not possible at this time to estimate the amount of loss or range of possible loss, if any, that might result from an adverse resolution of this action.

From time to time, we are a party to various other lawsuits, claims and other legal proceedings that arise in the ordinary course of our business. Management does not expect that the ultimate costs to resolve these matters will materially adversely affect our business, financial position, or results of operations.

ITEM 4. 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 trades on the Nasdaq Capital Market. In March 2011, following our reverse stock split, our stock temporarily traded under the symbol "INSMED" for a period of 20 days. The following table lists the high and low sale prices per share for our common stock on a quarterly basis as reported on the Nasdaq Capital Market for both 2012 and 2011. The first quarter 2011 prices have been adjusted for a one-for-ten reverse stock split that took place on March 2, 2011.

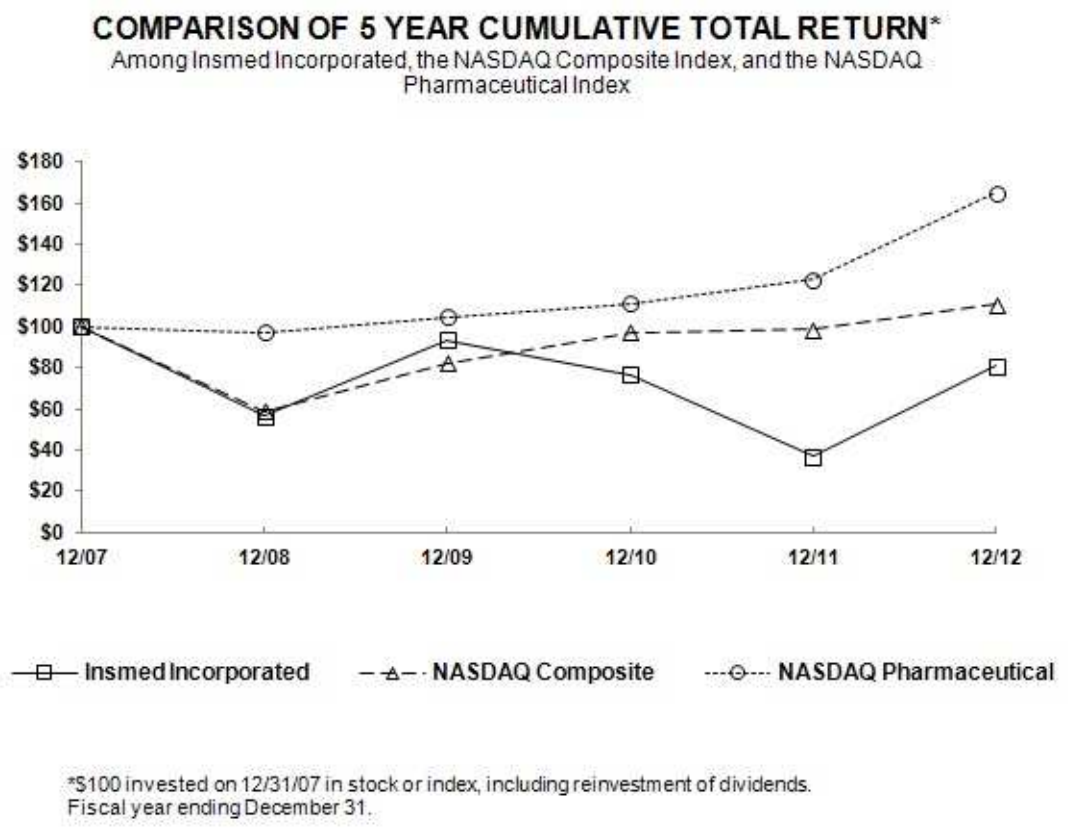
Fiscal Year 2012	High	Low
Fourth Quarter	$ 8.27	$ 4.44
Third Quarter	4.58	2.86
Second Quarter	4.93	2.66
First Quarter	5.50	3.04

Fiscal Year 2011	High	Low
Fourth Quarter	$ 5.23	$ 2.64
Third Quarter	12.62	3.20
Second Quarter	13.50	6.70
First Quarter	6.89	4.69

On February 28, 2013, the last reported sale price for our common stock on the Nasdaq Capital Market was $6.16 per share. As of February 28, 2013, there were 154 holders of record of our common stock.

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. Therefore, we do not currently expect to pay cash dividends from earnings. Any future determination as to the payment of dividends 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, as well as any contractual or other restrictions to which we may be subject.

PERFORMANCE GRAPH



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, 2012, 2011, 2010, 2009 and 2008. 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,				
	2012	2011	2010	2009	2008
	(in thousands, except per share data)				
Historical Statement of Operations Data:					
Revenues	$ -	$ 4,417	$ 6,921	$ 10,373	$ 11,699
Operating expenses:					
Research and development	29,781	28,623	4,702	9,017	20,855
General and administrative	12,657	11,523	10,311	10,030	5,255
Impairment loss	-	25,990	-	-	-
Total operating expenses	42,438	66,136	15,013	19,047	26,110
Operating loss	(42,438)	(61,719)	(8,092)	(8,674)	(14,411)
Gain on sale of asset, net	5	1	-	127,474	-
Investment income	1,822	2,064	1,845	808	500
Interest expense	(763)	(10)	(109)	(781)	(1,256)
Loss on investments	-	-	-	-	(500)
(Loss) income before income taxes	(41,374)	(59,664)	(6,356)	118,827	(15,667)
Income tax expense	-	-	(78)	(477)	-
Net (loss) income	(41,374)	(59,664)	(6,434)	118,350	(15,667)
Accretion of beneficial conversion feature	-	(9,175)	-	-	-
Net (loss) income attributable to common stockholders	$ (41,374)	$ (68,839)	$ (6,434)	$ 118,350	$ (15,667)
Basic and diluted net (loss) income attributable to common stockholders per share (1)	$ (1.56)	$ (2.95)	$ (0.49)	$ 9.31	$ (1.28)
Weighted average basic and diluted common shares outstanding (1)	26,545	23,348	13,250	12,712	12,213
Historical Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 90,782	$ 76,272	$ 108,049	$ 122,181	$ 2,397
Certificate of deposit	$ 2,153	$ 2,085	$ 2,176	$ 2,085	$ 2,085
Total assets	$ 153,561	$ 139,833	$ 196,265	$ 126,695	$ 4,758
Short-term debt ,net	$ 3,007	$ -	$ -	$ -	$ 1,615
Long-term debt, net	$ 16,221	$ -	$ -	$ -	$ 487
Net Stockholders' equity (deficit) (1)	$ 120,882	$ 134,267	$ 192,843	$ 123,914	$ (2,823)

(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 biopharmaceutical company focused on developing and commercializing inhaled therapies for patients battling serious lung diseases that are often life-threatening. Our lead product candidate, ARIKACE or liposomal amikacin for inhalation, is an inhaled antibiotic treatment that delivers a proven and potent anti-infective directly to the site of serious lung infections to improve the efficacy, safety and convenience of this therapeutic approach for patients.

Currently, we are conducting clinical trials for two initial indications for this product in orphan patient populations: a phase 3 clinical trial in CF patients who have lung infections caused by *Pseudomonas aeruginosa* (*Pseudomonas*) and a phase 2 clinical trial in patients who have lung infections caused by non-tuberculous mycobacteria (NTM). Our strategy is to continue to develop ARIKACE for additional indications beyond *Pseudomonas* in CF and NTM. Our primary development focus is to obtain regulatory approval for ARIKACE for these two initial indications and to prepare for commercialization initially in Europe and Canada and eventually in the US. If approved, ARIKACE will be the first once-a-day inhaled antibiotic treatment option available for these CF and NTM indications.

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. Our principal executive offices are located at 9 Deer Park Drive, Suite C, Monmouth Junction, New Jersey 08852 and our phone number is (732) 997-4600. Our Internet address is www.insmed.com. On March 2, 2011, we completed a one-for-ten reverse stock split of our common stock. Unless otherwise noted, the per share amounts in this Annual Report on Form 10-K give retroactive effect to the reverse stock split for all periods presented.

KEY COMPONENTS OF OUR STATEMENT OF OPERATIONS

Revenues

We did not recognize any revenue in 2012, and currently do not recognize any revenue from product sales or other sources. Our revenues in 2011 and 2010 consisted of cost recovery revenues from the use of IPLEX ® in an Expanded Access Program (EAP) we established in Italy to provide IPLEX ® to physicians for use in their patients with Amyotrophic Lateral Sclerosis (ALS) (this program was discontinued in December 2011), and an upfront license payment received from Eleison Pharmaceuticals, Inc. (Eleison) for the licensing of our lipid-complexed cisplatin and/or liposomal cisplatin products and technology to Eleison .

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, 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 ARIKACE 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 mainly 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.

Prior to 2011, we devoted substantially all of our resources to the research and development of a number of product candidates in our follow-on-biologics (FOB) platform and advancing our proprietary protein platform into niche markets with unmet needs. Since 2011, we have focused our development activities principally on our proprietary, advanced liposomal technology designed specifically for inhalation lung delivery. We are conducting three clinical trials: (1) a phase 3 trial in Europe and Canada in which we are evaluating ARIKACE in CF patients with *Pseudomonas* lung infections, (2) an open label extension study in which patients that complete the phase 3 trial have the option to receive ARIKACE for a period of two years and (3) a phase 2 trial in the US in which we are evaluating ARIKACE for NTM infections. Since our business combination with Transave, our research and development expenses for our ARIKACE program were approximately $44.0 million. We expect that our development efforts in 2013 and 2014 will principally relate to the use of ARIKACE in the CF and NTM indications.

Our clinical trials with ARIKACE 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, market research, 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.

Impairment Loss

Impairment loss consists of the write-down of the carrying amounts of in-process research and development (IPR&D) and Goodwill intangible assets. We use the multi-period excess earnings method (“MPEEM”) for calculating impairment loss, which is a form of the income approach to derive the fair value of IPR&D intangible and goodwill 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. We decided that a market based valuation approach was not appropriate for our financial reporting because we do not have operating revenues or net income. The income approach requires significant management judgment with respect to future volume, revenue and expense growth rates, changes in our working capital, appropriate discount rates and other assumptions and estimates. We believe the estimates and assumptions used in assessing impairment loss are consistent with our business plans. The use of different estimates and assumptions would increase or decrease the estimated fair value of our IPR&D, and might result in different effects on our results of operations. Our actual results of operations may differ from management's estimates used in assessing impairment loss.

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.

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 related to our debt and capital lease obligations.

RESULTS OF OPERATIONS

Comparison of Years Ended December 31, 2012 and 2011

Net loss attributable to common stockholders for the year ended December 31, 2012 was $41.4 million (or $1.56 per common share – basic and diluted) compared with a net loss of $68.8 million (or $2.95 per common share – basic and diluted) for the year ended December 31, 2011. The net loss attributable to stockholders in 2012 includes approximately $2.9 million in severance costs related to the termination of certain executives and employees. The net loss attributable to common stockholders in 2011 includes a $26.0 million non-cash impairment loss for the write-down of the carrying amounts our IPR&D and Goodwill intangible assets, a $9.2 million non-cash charge for the beneficial conversion feature of our previously outstanding Series B Preferred Stock issued in the Transave merger and approximately $1.2 million in expenses relating to our decision to discontinue use of our Richmond, Virginia facility.

Revenue

We did not recognize any revenue for the year-ended December 31, 2012. Our revenues in 2011 consisted of $3.4 million of cost recovery revenues from the use of IPLEX ® in an Expanded Access Program (EAP) we established in Italy to provide IPLEX ® to physicians for use in their patients with amyotrophic lateral sclerosis and a $1.0 million non-refundable upfront license payment received from Eleison Pharmaceuticals, Inc. for the licensing of our liposomal cisplatin products and technology . We recorded this revenue during 2011 as we had the contractual right to receive it and we have no continuing involvement under this licensing agreement.

Research and Development Expenses

Research and development expenses for the years ended December 31, 2012 and 2011, comprised the following:

	Year Ended December 31,		Increase (Decrease)	
	2012	2011	$	%
	(in thousands)			
Clinical development	$ 14,081	$ 16,835	$ (2,754)	-16%
Clinical manufacturing	7,254	4,790	2,464	51%
Regulatory and quality assurance	34	106	(72)	-68%
Compensation and related	8,412	6,892	1,520	22%
	$ 29,781	$ 28,623	$ 1,158	4%

Research and development expenses increased to $29.8 million in 2012 from $28.6 million in 2011. Despite an increase in clinical trial activity in 2012, our overall clinical development expenses decreased by $2.8 million. This decrease was primarily attributable to study start-up expenses incurred in 2011 related to the ARIKACE phase 3 clinical trial in a US CF patient population and the costs incurred to establish and initiate our phase 3 CF clinical trial in Europe and Canada. The 2012 clinical development costs include clinical trial expenses and enrollment milestones for our phase 3 CF clinical study in Europe and Canada, the open label CF extension study, as well as our phase 2 NTM clinical study in the US. Clinical manufacturing expenses increased by $2.5 million from 2011 to 2012 as we produced a greater number of ARIKACE lots for use in our studies. The decrease in regulatory and quality assurance expenses of $0.1 million in the year ended 2012 compared with 2011 was attributable to the regulatory planning associated with the clinical studies noted above. The $1.5 million increase in compensation and related expenses is attributable to increases in employee separation costs, including severance and related benefits, and facilities costs.

General and Administrative Expenses

General and administrative expenses increased to $12.7 million in 2012 from $11.5 million in 2011. The 2012 results included approximately $2.2 million in severance expenses related to the departure of several executives and employees. The 2011 results included $1.2 million in charges related to our decision to discontinue use of our Richmond, Virginia facility. In addition, total professional fees decreased by $0.7 million from 2011 to 2012 as a result of lower legal fees.

Impairment Loss

We recorded a $26.0 million non-cash impairment loss in 2011 due to the decline in the fair value of our in-process research and development, or IPR&D intangible and goodwill assets. This decline in fair value resulted from the impact of the clinical hold placed on our phase 3 studies of ARIKACE by the FDA in August 2011. In January 2012, the FDA lifted the clinical hold on ARIKACE in patients with NTM lung infections, and in May 2012, the FDA lifted the clinical hold on ARIKACE in the US for the treatment of CF patients with *Pseudomonas* lung infections.

Investment Income

Investment income decreased to $1.8 million in 2012 from $2.1 million in 2011. The $0.3 million decrease is a result of diminishing rates of return on our short-term investments during 2012 compared to 2011.

Interest Expense

Interest expense increased to $0.8 million during 2012 compared to $0.0 million in 2011. The $0.8 million increase was due to $20.0 million of borrowings ($10.0 million in June 2012 and $10.0 million in December 2012) under our Loan and Security Agreement we entered into in June 2012.

Accretion of Beneficial Conversion Feature

During March 2011, our stockholders approved a proposal to convert all of our outstanding Series B Preferred Stock into common stock. In connection with this approval, we recorded a $9.2 million non-cash charge in 2011 for the beneficial conversion feature of our previously outstanding Series B Preferred Stock. The charge resulted from the difference between the conversion price of the Series B Preferred Stock of $7.10 per share and its carrying value of $6.10 per share. The carrying value of the Series B Preferred Stock was based on its fair value at issuance, which was estimated using the common stock price reduced for a lack of marketability between the issuance date and the anticipated date of conversion.

Comparison of Years Ended December 31, 2011 and 2010

Net loss attributable to common stockholders for the year ended December 31, 2011 was $68.8 million (or $2.95 per common share – basic and diluted) compared with a net loss of $6.4 million (or $0.49 per common share – basic and diluted) for the year ended December 31, 2010. The net loss attributable to common stockholders in 2011 included a $26.0 million non-cash charge related to the impairment of our in process research and development and a $9.2 million non-cash charge for the beneficial conversion feature of our previously outstanding Series B Preferred Stock.

Revenue

For the year-ended December 31, 2011, revenues totaled $4.4 million, as compared with $6 . 9 million for the year-ended December 31, 2010. The $2.5 million reduction was primarily due to a year-over-year decrease of $3.5 million in cost recovery revenue from our IPLEX EAP in Europe, offset by $1.0 million in license fees from the licensing of patent technology related to our CISPLATIN Lipid Complex. Our IPLEX EAP was discontinued in 2011.

Research and Development Expenses

Research and development expenses increased to $28.6 million in 2011 from $4.7 million in 2010. The increase of $23.9 million in 2011 is primarily attributable to the development of ARIKACE and the manufacturing of product to support clinical studies. Clinical development expenses increased by $15.6 million in 2011 as compared with 2010 as a result of study initiation and start-up fees for ARIKACE plus the expenses for a preclinical toxicology study associated with the ARIKACE development program. In addition, a $4.5 million increase in clinical manufacturing expenses from 2011 to 2010 was attributable to the manufacturing of ARIKACE for use in our studies.

We also incurred greater compensation and related expenses of $4.4 million as a result of increased headcount associated with the development of ARIKACE. In fact, overall research and development headcount increased from approximately 11 as of December 31, 2010 to 28 as of December 31, 2011.

General and Administrative Expenses

General and administrative expenses increased to $11.5 million in 2011 from $10.3 million in 2010. The $1.2 million increase was due primarily to a $1.2 million charge in the fourth quarter of 2011 resulting from the closure of our Richmond, Virginia facility.

Impairment Loss

In 2011 we recorded a $26.0 million non-cash impairment loss resulting from the decline in the fair value of our IPR&D intangible and goodwill assets, due to the material impact of the temporary clinical hold on our ARIKACE development program. In January 2012, the FDA lifted the clinical hold on ARIKACE in patients with NTM lung infections. In May 2012, the FDA lifted the clinical hold on ARIKACE in the US for the treatment of CF patients with *Pseudomonas* lung infections.

Investment Income and Interest Expense

Investment income, net of interest expense, increased to $2.1 million in 2011 from $1.7 million in 2010. The $0.3 million increase is a result of improved returns on our short-term investments despite a decrease in overall short-term investment balances year over year. The reduction in interest expense in 2011 compared with 2010 was entirely due to the elimination of convertible notes, which were fully repaid in March 2010.

Accretion of Beneficial Conversion Feature

In 2011, we recorded a $9.2 million non-cash charge for the beneficial conversion feature of our then outstanding Series B Preferred Stock. The charge resulted from the difference between the conversion price of the Series B Preferred Stock of $7.10 per share and its carrying value of $6.10 per share. The carrying value of the Series B Preferred Stock was based on its fair value at issuance, which was estimated using the common stock price reduced for a lack of marketability between the issuance date and the anticipated date of conversion.

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 (“FOB”) platform to Merck in 2009 and from revenues related to sales of product and our IPLEX EAP, 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 few years.

As of December 31, 2012, we had total cash, cash equivalents, and a certificate of deposit on hand of $92.9 million, consisting of $90.7 million in cash and cash equivalents and $2.2 million in a certificate of deposit, as compared with $78.4 million of cash, cash equivalents, short term investments and a certificate of deposit on hand as of December 31, 2011, an increase of $14.5 million. The $14.5 million (net) increase was due to our financing activities during 2012, which included $20.0 million of proceeds from our debt financing and $25.7 million of proceeds from the issuance of common stock, which were partially offset by the use of $31.0 million in operations. Our working capital was $75.7 million as of December 31, 2012, which excludes our certificate of deposit of $2.2 million that matures in July 2013.

We believe we currently have sufficient funds to meet our financial needs for 2013. 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. In addition, we may determine to raise capital opportunistically. 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.

Cash Flows

Net cash used in operating activities was $31.0 million, $30.2 million and $7.7 million for the years ended December 31, 2012, 2011 and 2010, respectively. The net cash used in operating activities during 2012 and 2011 was primarily for the clinical development of our lead product candidate, ARIKACE, which included the advancement of ARIKACE in three clinical trials. The $22.5 million increase in net cash used in operating activities in 2011 as compared to 2010 related primarily to the initiation of two clinical trials for the study of ARIKACE.

Net cash provided by investing activities was $61.5 million, $34.4 million and $6.0 million for the years ended December 31, 2012, 2011 and 2010, respectively. The net cash provided by investing activities in 2012 was primarily a result of the net sales of short-term investments of $61.8 million. The net cash provided by investing activities in 2011 resulted from $35.3 million of net sales of short-term investments that were partially offset by fixed asset purchases of $1.0 million that were primarily for leasehold improvements. The net cash provided by investing activities in 2010 was primarily a result of $12.7 million of net sales of short-term investments that were partially offset by $6.7 million of cash consideration paid to stockholders as a result of our merger with Transave.

Net cash provided by (used in) financing activities was $45.4 million, ($0.1) million and ($0.2) million for the years ended December 31, 2012, 2011 and 2010, respectively. Net cash provided by financing activities in 2012 included $20.0 million of proceeds from the issuance of debt and $25.7 million of proceeds from the issuance of common stock registered in a direct public offering. Net cash used in financing activities in 2011 was primarily a result of payments on capital lease obligations. Net cash used in financing activities in 2010 was due to the final repayment of the 2005 convertible notes.

On June 29, 2012, we and our domestic subsidiaries, as co-borrowers, entered into a Loan and Security Agreement that allowed us to borrow up $20.0 million in $10.0 million increments (“Loan Agreement”). We borrowed the first and second $10.0 million increments by signing two Secured Promissory Notes (“Notes A and B”) on June 29, 2012 and December 27, 2012, respectively. Notes A and B bear interest at 9.25%. Note A is to be repaid over a 42-month period with the first twelve monthly payments representing interest only followed by thirty monthly equal payments of principal and interest. Note B is to be repaid over a 36-month period with the first six monthly payments representing interest only followed by thirty monthly equal payments of principal and interest. The interest only period is extendable to December 31, 2013, contingent upon completion of certain ARIKACE-related development milestones. The principal monthly repayments for Notes A and B are scheduled to begin on August 1, 2013 and end on January 1, 2016. In connection with the Loan Agreement, we granted the lender a first position lien on all of our assets, excluding intellectual property. Prepayment of the loans made pursuant to the Loan Agreement is subject to penalty and we are required to pay an “end of term” charge of $390,000.

Contractual Obligations

We have two operating leases for office and laboratory space located in Monmouth Junction, NJ that terminate on December 31, 2014. Future minimum rental payments under these two leases total approximately $1.4 million. We continue to lease office space in Richmond, VA where our corporate headquarters were previously located. Future minimum rental payments under this lease total approximately $1.9 million. During 2011, we recorded a net present value charge of $1.2 million in general and administrative expenses associated with vacating the Richmond, VA facility.

We executed two secured promissory notes totaling $20.0 million; $10.0 million in June 2012 and $10.0 million in December 2012. We also entered into three capital leases for lab equipment and leasehold improvements with monthly payments through December 2014. As of December 31, 2012, future payments under the two promissory notes, the capital leases and minimum future payments under non-cancellable operating leases are as follows:

	As of December 31, 2012				
		Payments Due By Period			
	Total	Less than 1 year	1-3 Years	4-5 Years	After 5 Years
			(In thousands)		
Debt obligations					
Debt maturities	$ 20,000	$ 3,007	$ 16,205	$ 788	$ -
Contractual interest	3,545	1,762	1,777	6	-
Capital lease obligations	-			-	
Debt maturities	166	102	64	-	-
Contractual interest	1	1	-	-	-
Operating leases	3,312	1,188	1,699	425	
Purchase obligations	-	-	-	-	-
Total contractual obligations	$ 27,024	$ 6,060	$ 19,745	$ 1,219	$ -

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, and (c) contracts that are entered into in the ordinary course of business which are not material in the aggregate in any period presented above.

We currently have a licensing agreement with PARI for use of the optimized eFlow Nebulizer System for delivery of ARIKACE in treating patients with CF, bronchiectasis and 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 (which occurred in 2012), first acceptance of MAA submission (or equivalent) in the US of ARIKACE and the device, first receipt of marketing approval in the US for ARIKACE and the device, and first receipt of marketing approval in a major EU country for ARIKACE and the device, and NDA acceptance and regulatory approval of ARIKACE. In addition, PARI is entitled to receive royalty payments on commercial sales of ARIKACE pursuant to the licensing agreement.

In 2005 and 2009, we entered into a 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 its ARIKACE product. If ARIKACE 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 sales milestones are met within 5 years of the drug commercialization approval in the US, we would owe an additional $3.9 million in additional payments. Since there is significant development risk associated with ARIKACE, we have not accrued these obligations.

In 2009 and 2012, we entered into a cooperative research and development agreement (CRADA) with National Institutes of Allergy and Infectious Diseases (NIAID) to design and conduct our phase 2 study of ARIKACE in patients with NTM. NIAID has also agreed to provide biostatistical advisory input in connection with the phase 2 NTM study. If we decide not to continue with the commercialization of ARIKACE in NTM, NIAID will have the right to complete the clinical trial. Further NIAID may elect to pursue its rights to obtain license rights to certain inventions made under the CRADA.

Future Funding Requirements

We may need to raise additional capital to fund our operations and to develop and commercialize ARIKACE. Our future capital requirements may be substantial and will depend on many factors, including:

- the decisions of the FDA and EMA with respect to our applications for marketing approval of ARIKACE in the US and Europe; the costs of activities related to the regulatory approval process; and the timing of approvals, if received;
- the timing and cost of our anticipated clinical trials of ARIKACE for the treatment of adult patients with CF;
- the cost of putting in place the sales and marketing capabilities necessary to be prepared for a potential commercial launch of ARIKACE, if approved;
- the cost of filing, prosecuting and enforcing patent claims;
- the costs of our manufacturing-related activities;
- the costs associated with commercializing ARIKACE 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 June 2012, we filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission. This shelf registration statement permits us to offer, from time to time, any combination of common stock, preferred stock, debt securities and warrants of up to an aggregate of $75.0 million. In October 2012, we issued approximately $25.7 million worth of common stock utilizing the shelf registration statement. We believe we currently have sufficient funds to meet our financial needs for 2013. 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. In addition, we may determine to raise capital opportunistically. 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 revenue from ARIKACE. 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, ARIKACE.

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, beneficial conversion charge, 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 ARIKACE 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 mainly 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

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.

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.

Beneficial Conversion Charge

When issuing debt or equity securities that are convertible into our common stock at a discount from the fair value of our common stock at the date the debt or equity financing is committed, we are required to record a beneficial conversion charge in accordance with Accounting Standards Codification 470-20 on the commitment date (the conversion date). The beneficial conversion charge is measured as the difference between the fair value of the securities at the time of issue and the fair value of the common stock at the commitment date. We record the beneficial conversion charge as a non-cash charge to earnings. In 2011, we recorded a beneficial conversion charge of $9.2 million for the conversion of our previously outstanding Series B Preferred Stock (issued in the Transave merger) into common stock. See Note 3 of the consolidated financial statements for further information about the beneficial conversion feature.

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. 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 deemed to be granted outside of the Company's 2000 Stock Incentive Plan, the Company uses liability accounting. These awards are classified as a liability and are 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 10 "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, 2012 and 2011 (no stock options were granted during 2010).

	2012	2011
Volatility	96.2%	111.6%
Risk-free interest rate	0.7%	0.9%
Dividend yield	0.0%	0.0%
Expected option term (in years)	6.25	6.25

For the years ended December 31, 2012 and 2011, 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 and Goodwill

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

Recently Adopted Accounting Pronouncements

In June 2011, an Accounting Standards Update was issued that eliminates the current option to report other comprehensive income and its components in the statement of stockholders' equity. Instead, an entity will be required to present items of net income (loss) and other comprehensive income (loss) in one continuous statement or in two separate, but consecutive statements. This standard became effective for us on January 1, 2012. As this accounting standard relates only to the presentation of other comprehensive income (loss), the adoption of the standard did not have an impact on our consolidated financial statements.

In May 2011, an amendment to an accounting standard was issued that amends the fair value measurement guidance and includes some expanded disclosure requirements. The most significant change is the disclosure information required for Level 3 (see Note 2) measurements based on unobservable inputs. This amendment became effective for us on January 1, 2012 and its adoption did not impact our consolidated financial statements.

Recently Issued Accounting Pronouncements

In February 2013, an Accounting Standards Update was issued that requires companies to present either in a single note or parenthetically on the face of the financial statements, the effect of significant amounts reclassified from each component of accumulated other comprehensive income (loss) based on its source and the income statement line items affected by the reclassification. This guidance is effective for annual and interim reporting periods beginning after December 15, 2012. We believe the adoption of this standard will not have a material impact on our consolidated financial statements.

In July 2012, an Accounting Standards Update was issued that allows companies to assess qualitative factors to determine the likelihood of indefinite-lived intangible asset impairment and whether it is necessary to perform the quantitative impairment test currently required. This guidance is effective for annual and interim impairment tests performed for fiscal years beginning after September 15, 2012, with early adoption permitted. We believe the adoption of this standard will not have a material impact on our consolidated financial statements.

In December 2011, an Accounting Standards Update was issued that requires disclosure of information about offsetting and related arrangements to enable users of our consolidated financial statements to understand the effect of those arrangements on the our financial position. The new guidance is effective for annual reporting periods beginning on or after January 1, 2013, and interim periods within those annual periods. The disclosures required are to be applied retrospectively for all comparative periods presented. Upon adoption, we do not expect that this standard will materially impact our disclosures included in our consolidated financial statements.

ITEM 7A. QUANTITA TIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As of December 31, 2012, 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, 2012, we had $20.0 million of fixed rate borrowings in the form of two secured promissory notes that bear interest at 9.25% outstanding under a Loan and Security Agreement we entered into in June 2012. If a 10% change in interest rates were to have occurred on December 31, 2012, 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 or British Pounds. Fluctuations in foreign currency exchange rates do not materially effect on our results of operations. During 2012, 2011 and 2010, 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, 2012. 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. In light of the material weakness over the administration, accounting and oversight of our Amended and Restated 2000 Stock Incentive Plan, further described below, we concluded that our disclosure controls and procedures were ineffective as of December 31, 2012.

As a result of the identification of the material weakness, management performed additional analyses and other procedures to ensure its consolidated financial statements were prepared in accordance with accounting principles generally accepted in the US. These additional analyses and procedures included, among other things, expansion of our normal year-end closing and testing procedures and deployment of significant in-house and external resources. Based on the additional procedures performed, management, including our Chief Executive Officer and Chief Financial Officer, concluded that the consolidated financial statements included in this Form 10-K present fairly, in all material respects, our financial position, results of operations and cash flows for the periods presented.

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 U.S. 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, 2012, based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control — Integrated 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 the company's annual or interim financial statements will not be prevented or detected on a timely basis. Based on management's assessment, including consideration of the control deficiencies discussed below, management concluded that the company's internal control over financial reporting was ineffective as of December 31, 2012, due to the fact that there was a material weakness in our internal control over the administration, accounting and oversight of its 2000 Stock Incentive Plan. Specifically, in connection with a recent review of our equity compensation grants, we determined that we had inadvertently exceeded the annual per-person sub-limits applicable to grants of equity awards provided for by our 2000 Stock Incentive Plan. During the two years ended December 31, 2012, we granted equity compensation to employees and directors relating to an aggregate of 1.4 million shares of common stock in excess of such sub-limits, which resulted in additional stock based compensation expense of $0.5 million and a liability of $1.2 million in the consolidated financial statements for the period ending and as of December 31, 2012. Additionally, on January 2, 2013, we granted a stock option that exceeded the applicable sub-limit by 10,000 shares. We have not exceeded the overall 3,925,000 share reserve currently provided for by the 2000 Stock Incentive Plan and approved by shareholders, whether as a result of previously-issued awards or currently outstanding awards.

Remediation Plan

Management and our Board of Directors are actively engaged in implementing a remediation plan to address the material weakness over the administration, accounting and oversight of our 2000 Stock Incentive Plan. We recently hired a new Chief Financial Officer and a new Senior Vice President of Human Resources, and we added a senior director to our finance staff which we believe will help strengthen our internal controls. Additional remediation efforts we expect to implement include, among other things, modification of certain forms and processes, training of certain personnel, possible rotation of Board members to different committees and a review of each of the charters for our Board committees.

Pursuant to our remediation plan, on March 15, 2013, our compensation committee of the Board recommended and the Board approved an amendment to the 2000 Stock Incentive Plan to replace the three individual annual per person equity compensation limits with a single aggregate stock option, performance share and restricted stock sub-limit of 1,500,000 shares. We did not change the overall share reserve for the 2000 Stock Incentive Plan of 3,925,000 shares, which was approved by our shareholders in 2011.

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 2013 annual meeting of stockholders to be filed with the SEC.

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 2013 annual meeting of stockholders to be filed with the SEC.

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 2013 annual meeting of stockholders to be filed with the SEC.

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 2013 annual meeting of stockholders to be filed with the SEC.

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 2013 annual meeting of stockholders to be filed with the SEC.

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 F-1:

(i) Reports of Independent Registered Public Accounting Firm

(ii) Consolidated Balance Sheets as of December 31, 2012 and 2011

(iii) Consolidated Statements of Comprehensive Loss for the Years Ended December 31, 2012, 2011 and 2010

(iv) Consolidated Statements of Stockholders' Equity for the Years Ended December 31, 2012, 2011 and 2010

(v) Consolidated Statements of Cash Flows for the Years Ended December 31, 2012, 2011 and 2010

(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 the 18 th day of March, 2013.

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 the 18 th day of March, 2013.

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/ Al Altomari Al Altomari	Director
/s/ Steinar J. Engelsen, M.D. Steinar J. Engelsen, M.D.	Director
/s/ Richard S. Kollender Richard S. Kollender	Director
/s/ Melvin Sharoky, M.D. Melvin Sharoky, M.D.	Director
/s/ Randall W. Whitcomb, M.D. Randall W. Whitcomb, 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, 2012 and 2011, 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, 2012. 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, 2012 and 2011, and the consolidated results of its comprehensive loss and its cash flows for each of the three years in the period ended December 31, 2012, in conformity with US 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, 2012, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 18, 2013 expressed an adverse opinion thereon.

/s/ Ernst & Young LLP

MetroPark, New Jersey
March 18, 2013

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, 2012, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (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.

A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis. The following material weakness has been identified and included in management's assessment. Management has identified a material weakness in its internal controls over the administration, accounting and oversight of its 2000 Stock Incentive Plan. We also 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, 2012 and 2011, and the related consolidated statements of comprehensive loss, stockholders' equity, and cash flows for each of the three years ended December 31, 2012. This material weakness was considered in determining the nature, timing and extent of audit tests applied in our audit of the 2012 consolidated financial statements, and this report does not affect our report dated March 18, 2013, which expressed an unqualified opinion on those financial statements.

In our opinion, because of the effect of the material weakness described above on the achievement of the objectives of the control criteria, Insmed Incorporated has not maintained effective internal control over financial reporting as of December 31, 2012, based on the COSO criteria.

/s/ Ernst & Young LLP

MetroPark, New Jersey
March 18, 2013

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

	December 31, 2012	December 31, 2011
Assets		
Current assets:		
Cash and cash equivalents	$ 90,782	$ 14,848
Short-term investments	-	61,424
Certificate of deposit	2,153	-
Accounts receivable	-	757
Prepaid expenses and other current assets	643	370
Total current assets	93,578	77,399
Certificate of deposit	-	2,085
In-process research and development	58,200	58,200
Other assets	117	212
Fixed assets, net	1,666	1,937
Total assets	$ 153,561	$ 139,833
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 7,060	$ 2,334
Accrued expenses	2,933	800
Accrued compensation	2,207	795
Accrued lease expense, current	295	278
Deferred rent	149	156
Capital lease obligations, current	96	114
Current portion of long term debt	3,007	-
Total current liabilities	15,747	4,477
Accrued lease expense, long-term	647	923
Capital lease obligations, long-term	64	166
Debt, long-term	16,221	-
Total liabilities	32,679	5,566
Commitments and contingencies	-	-
Stockholders' equity:		
Common stock; $.01 par value; 500,000,000 authorized shares, 31,488,204 and 24,833,301 issued and outstanding shares at December 31, 2012 and 2011, respectively	315	248
Additional paid-in capital	455,325	427,743
Warrant to purchase 329,932 shares of common stock for $2.94 per share at December 31, 2012	790	-
Accumulated deficit	(335,548)	(294,174)
Accumulated other comprehensive income:		
Unrealized gain on investments, net of taxes	-	450
Total stockholders' equity	120,882	134,267
Total liabilities and stockholders' equity	$ 153,561	$ 139,833

See accompanying notes to audited consolidated financial statements

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

	Years ended December 31, 2012	2011	2010
License fees	$ -	$ 1,002	$ 4
Other expanded access program income, net	-	3,415	6,917
Total revenues	-	4,417	6,921
Operating expenses:			
Research and development	29,781	28,623	4,702
General and administrative	12,657	11,523	10,311
Impairment loss	-	25,990	-
Total operating expenses	42,438	66,136	15,013
Operating loss	(42,438)	(61,719)	(8,092)
Investment income	1,822	2,064	1,845
Interest expense	(763)	(10)	(109)
Gain on sale of asset, net	5	1	-
Loss before income taxes	(41,374)	(59,664)	(6,356)
Provision for income taxes	-	-	78
Net loss	(41,374)	(59,664)	(6,434)
Accretion of beneficial conversion charge	-	(9,175)	-
Net loss attributable to common stockholders	$ (41,374)	$ (68,839)	$ (6,434)
Basic and diluted net loss attributable to common stockholders per share	$ (1.56)	$ (2.95)	$ (0.49)
Weighted average basic and diluted common shares outstanding	26,545	23,348	13,250
Net loss attributable to common stockholders	$ (41,374)	$ (68,839)	$ (6,434)
Comprehensive loss:			
Unrealized gains on investments, net of taxes	-	450	993
Comprehensive loss attributable to common stockholders	$ (41,374)	$ (68,389)	$ (5,441)

See accompanying notes to audited consolidated financial statements

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

	Common Stock		Preferred Stock		Warrant		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance at December 31, 2009	13,021	$ 1,302	-	$ -	-	$ -	$ 350,243	$ (228,076)	$ 445	$123,914
Comprehensive loss:										
Net loss								(6,434)		(6,434)
Unrealized gain (loss) on investment, net of taxes									548	548
Issuance of common stock upon issuance of restricted stock awards	39	4					-	-	-	4
Issuance of common stock upon merger	2,594	259					18,160	-	-	18,419
Issuance of preferred stock upon merger			9,175	918			55,108	-	-	56,026
Stock compensation expense		-					366	-	-	366
Balance at December 31, 2010	15,654	1,565	9,175	918	-	-	423,877	(234,510)	993	192,843
Comprehensive loss:										
Net loss								(59,664)		(59,664)
Unrealized gain (loss) on investment, net of taxes									(543)	(543)
Total comprehensive loss										
1 for 10 reverse stock split		(2,235)					2,235			0
Exercise of stock options	5	-					32	-	-	32
Conversion of preferred stock into common stock	9,174	918	(9,175)	(918)				-	-	
Stock compensation expense		-					1,599	-	-	1,599
Balance at December 31, 2011	24,833	248	-	-	-	-	427,743	(294,174)	450	134,267
Comprehensive loss:										
Net loss								(41,374)		(41,374)
Unrealized gain (loss) on investment, net of taxes									(450)	(450)
Exercise of stock options	30	1					213	-	-	214
Net proceeds from issuance of common stock	6,304	63					25,595			25,658
Issuance of common stock for vesting of RSUs	321	3					(3)	-	-	-
Fair value of warrant granted in connection with debt financing					330	790				790
Stock compensation expense		-					1,777	-	-	1,777
Balance at December 31, 2012	31,488	$ 315	-	$ -	330	$ 790	$ 455,325	$ (335,548)	$ -	$120,882

See accompanying notes to audited consolidated financial statements

INSMED INCORPORATED
Consolidated Statements of Cash Flows
(in thousands)

	Years ended December 31, 2012	2011	2010
Operating activities			
Net loss	$ (41,374)	$ (59,664)	$ (6,434)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	561	343	54
Stock based compensation expense	2,981	1,599	366
Gain on sale of asset, net	(5)	(1)	-
Gain on sale of short-term investments, net	(833)	-	-
Impairment loss	-	25,990	-
Amortization of debt discount and debt issuance costs	236	-	-
Accrual of the end of term charge on the debt	44	-	-
Changes in operating assets and liabilities:			
Accounts receivable	757	(286)	19
Income tax receivable	-	-	2,023
Prepaid expenses and other assets	(180)	(214)	(78)
Accounts payable	4,726	884	(2,750)
Accrued expenses and deferred rent	922	667	(1,127)
Accrued lease expenses	(259)	1,201	-
Accrued compensation	1,412	(322)	201
Deferred revenue	-	(402)	4
Net cash used in operating activities	(31,012)	(30,205)	(7,722)
Investing activities			
Cash consideration for merger, net of cash acquired	-	-	(6,733)
Purchase of fixed assets	(290)	(979)	-
Proceeds from sale of asset	5	-	-
Sales of short-term investments	81,464	36,500	115,153
Purchases of short-term investments	(19,657)	(1,161)	(102,462)
Net cash provided by investing activities	61,522	34,360	5,958
Financing activities			
Payments on capital lease obligations	(120)	(82)	(6)
Proceeds from issuance of debt	20,000	-	-
Repayment of convertible notes	-	-	(231)
Proceeds from issuance of common stock	25,658	-	-
Proceeds from exercise of stock options	214	32	-
Payment of debt issuance costs	(328)	-	-
Other	-	-	4
Net cash provided by (used in) financing activities	45,424	(50)	(233)
Increase (decrease) in cash and cash equivalents	75,934	4,105	(1,997)
Cash and cash equivalents at beginning of period	14,848	10,743	12,740
Cash and cash equivalents at end of period	$ 90,782	$ 14,848	$ 10,743
Supplemental disclosures of cash flow information:			
Cash paid for interest	$ 398	$ 10	$ -
Cash received for taxes, net	$ -	$ -	$ (1,884)
Supplemental disclosures of non-cash investing and financing activities:			
Capital lease obligations incurred	-	$ 198	-
Unrealized (gain) loss on investments	$ (450)	$ (543)	$ 548
Accretion of beneficial conversion charge	-	$ (9,175)	-
Fair value of warrant granted in connection with debt financing	$ 790	-	-
Conversion of Series B preferred stock into common stock	-	$ 918	-
Issuance of common stock upon merger	-	-	$ 18,419
Issuance of preferred stock upon merger	-	-	$ 56,026

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 biopharmaceutical company focused on developing and commercializing inhaled therapies for patients battling serious lung diseases that are often life threatening. The Company's lead product candidate, ARIKACE ®, or liposomal amikacin for inhalation, is an inhaled antibiotic treatment that delivers a proven and potent anti-infective directly to the site of serious lung infections to improve the efficacy, safety and convenience of this therapeutic approach for patients.

Currently, the Company is conducting clinical trials of ARIKACE for two initial indications in orphan patient populations: a phase 3 clinical trial in cystic fibrosis (CF) patients who have lung infections caused by *Pseudomonas aeruginosa* (*Pseudomonas*) and a phase 2 clinical trial in patients who have lung infections caused by non-tuberculous mycobacteria (NTM). The Company's strategy is to continue to develop ARIKACE for additional indications beyond *Pseudomonas* in CF and NTM. The Company's primary development focus is to obtain regulatory approval for ARIKACE for these two initial indications and to prepare for commercialization initially in Europe and Canada and eventually in the United States (US). If approved, ARIKACE will be the first once-a-day inhaled antibiotic treatment option available for these CF and NTM indications.

The Company was incorporated in the Commonwealth of Virginia on November 29, 1999. On December 1, 2010, the Company completed a business combination with Transave, Inc. (Transave), 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. The integration with Transave was completed in 2011. The Company's continuing operations are based on the technology and products historically developed by Transave. The Company's principal executive offices are located in Monmouth Junction, New Jersey.

Basis of Presentation - The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries, Transave, LLC, Insmed Pharmaceuticals, Incorporated, Insmed Limited, and Celtrix Pharmaceuticals, Incorporated (Celtrix). All significant intercompany balances and transactions 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 that it believes are reasonable under the circumstances. The amounts of assets and liabilities reported in the Company's balance sheets and the amounts of revenue and expenses reported for each periods presented are effected by estimates and assumptions, which are used for, but not limited to, the accounting for revenue recognition, stock-based compensation, income taxes, loss contingencies, the beneficial conversion charge, the warrant fair value calculation, impairment of intangibles and long lived assets and accounting for research and development costs. Actual results could differ from those estimates.

Prior Period Reclassifications - Certain amounts in the prior years' consolidated financial statements have been reclassified to conform to the current-year presentation. Specifically, the Company allocated a portion of certain operating expenses from general and administrative expense to research and development expense in 2012 and recast prior year amounts to conform to the current year presentation for comparability purposes.

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 related to our debt and capital lease obligations.

Cash, Cash Equivalents and Short-Term Investments - The Company considers cash equivalents to be highly liquid investments with maturities of three months or less from the date of purchase. Short-term investments were available for sale and consisted primarily of short-term municipal bonds, U. S. treasuries and mutual funds. These securities were carried at fair value of the investment based on quoted market prices. The cost of the specific security sold is used to compute the gain or loss on the sale of the securities sold.

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 seven years are used for computer equipment, 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, such as lab equipment, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be 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 and Goodwill - 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. 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, whi 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.
- 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 in the tables below 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. Financial instruments in Level 2 generally include municipal bonds listed in secondary markets.

The following table presents assets and liabilities measured at fair value as of December 31, 2012 and December 31, 2011 (in thousands).

	Fair Value Measurements at Reporting Date Using			
	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Quoted Prices in Inactive Markets for Identical Assets (Level 2)	Significant Unobservable Inputs (Level 3)
As of December 31, 2012:				
Assets:				
Cash and cash equivalents	$ 90,782	$ 90,782	$ -	$ -
Certificate of deposit	2,153	2,153	-	-
	$ 92,935	$ 92,935	$ -	$ -
As of December 31, 2011:				
Assets:				
Cash and cash equivalents	$ 14,848	$ 14,848	$ -	$ -
Mutual funds	56,163	56,163	-	-
Government agency bonds	5,261	-	5,261	-
Certificate of deposit	2,085	2,085	-	-
	$ 78,357	$ 73,096	$ 5,261	$ -

The Company's cash and cash equivalents and short-term investments, excluding government agency bonds, 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. The Company's investment in government agency bonds permitted daily redemption and the fair values of these investments are based upon the quoted prices in inactive markets by the holding financial institutions. The 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 certificate of deposit matures in July 2013.

We recognize transfers between levels within the fair value hierarchy, if any, at the end of each quarter. There were no significant transfers in or out of Level 1, Level 2 or Level 3 during 2012. During 2011, approximately $27.0 million was transferred from Level 2 assets into Level 1 to be utilized in the Company's operating activities.

As of December 31, 2012, the Company held no securities that were in an unrealized loss or gain position. During 2012, the Company realized a net gain of $0.8 million from the sale of short term investments.

As of December 31, 2011, the Company held two securities that were in an unrealized loss position with a total estimated fair value of $12.6 million and a gross unrealized loss of approximately $0.2 million. The net unrealized gain of $0.5 million is reported in accumulated other comprehensive income in the stockholder's equity section of the Company's balance sheet. Unrealized gains and losses for 2011 are as follows (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Mutual funds	$ 55,718	$ 652	$ (207)	$ 56,163
Government agency bonds	5,256	5	-	5,261
	$ 60,974	$ 657	$ (207)	$ 61,424

The Company reviews the status of each security quarterly to determine whether an other-than-temporary impairment has occurred. In making our determination, we consider 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) our ability and intent to retain the investment for a sufficient period of time for it to recover.

Concentration of Credit Risk - Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash, cash equivalents and short-term investments. The Company places its cash equivalents with high credit-quality financial institutions and invests 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 product candidate is performed by a sole manufacturer. The inability of the suppliers or manufacturer 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 – The Company's revenues in 2011 were from (1) $3.4 million of cost recovery revenues from the use of IPLEX ® in an Expanded Access Program (EAP) the Company established in Italy to provide IPLEX ® to physicians for use in their patients with Amyotrophic Lateral Sclerosis (ALS) (this program was discontinued in December 2011), and (2) a $1.0 million non-refundable upfront license payment received from Eleison Pharmaceuticals, Inc. (Eleison") for the licensing of the Company's lipid-complexed cisplatin and/or liposomal cisplatin products and technology to Eleison . We recorded this revenue during 2011 as we had the contractual right to receive it and we have no continuing involvement under this licensing agreement.

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.

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 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. 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 our research and development functions, and other internal operating expenses, the cost of manufacturing our 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 ARIKACE 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 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. 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 deemed to be granted outside of the Company's 2000 Stock Incentive Plan, the Company uses liability accounting. These awards are classified as a liability and are 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 10, 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, we take 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 our valuation allowance, we record 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 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, 2012 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 Income (Loss) Per Common Share - Basic net income (loss) per common share is computed by dividing net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding during the period. Diluted net income (loss) per common share is computed by dividing net income (loss) attributable to common stockholders by the weighted average number of common shares and other dilutive securities outstanding during the period. Potentially dilutive securities from stock options, the restricted stock units and the warrant would be antidilutive as the Company incurred a net loss. 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 attributable to common stockholders used to compute basic net income (loss) per share for the years ended December 31, 2012, 2011 and 2010.

	Year Ended December 31,		
	2012	**2011**	**2010**
	(in thousands except per share amounts)		
Numerator:			
Net income (loss) attributable to common stockholders	$ (41,374)	$ (68,839)	$ (6,434)
Denominator:			
Weighted average common shares used in calculation of basic net income (loss) per share:	26,545	23,348	13,250
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 income (loss) per share	26,545	23,348	13,250
Net income (loss) attributable to common stockholders per share:			
Basic and Diluted	$ (1.56)	$ (2.95)	$ (0.49)

The following potentially dilutive securities have been excluded from the computations of diluted weighted-average common shares outstanding as of December 31, 2012, 2011 and 2010 as their effect would have been anti-dilutive (in thousands).

	2012	2011	2010
Warrants to purchase common stock	330	158	158
Stock options to purchase common stock	1,818	892	214
Restricted stock and restricted stock units	216	487	-

Segment Information - The Company currently operates in one business segment, which is the development and commercialization of inhaled therapies for patients with serious lung infections. 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.

Recently Adopted Accounting Pronouncements - In June 2011, an Accounting Standards Update was issued that eliminates the current option to report other comprehensive income (loss) and its components in the statement of stockholders' equity. Instead, an entity will be required to present items of net income and other comprehensive income (loss) in one continuous statement or in two separate, but consecutive, statements. This standard became effective for the Company on January 1, 2012. As this accounting standard relates only to the presentation of other comprehensive income (loss), the adoption of the standard did not have an impact on the Company's consolidated financial statements.

In May 2011, an amendment to an accounting standard was issued that amends the fair value measurement guidance and includes some expanded disclosure requirements. The most significant change is the disclosure information required for Level 3 (see Note 2) measurements based on unobservable inputs. This amendment became effective for the Company on January 1, 2012 and its adoption did not impact the Company’s consolidated financial statements.

Recently Issued Accounting Pronouncements - In February 2013, an Accounting Standards Update that requires companies to present either in a single note or parenthetically on the face of the financial statements, the effect of significant amounts reclassified from each component of accumulated other comprehensive income (loss) based on its source and the income statement line items affected by the reclassification. This guidance is effective for annual and interim reporting periods beginning after December 15, 2012. The Company believes the adoption of this standard will not have a material impact on its consolidated financial statements.

In July 2012, an Accounting Standards Update was issued that allows companies to assess qualitative factors to determine the likelihood of indefinite-lived intangible asset impairment and whether it is necessary to perform the quantitative impairment test currently required. This guidance is effective for annual and interim impairment tests performed for fiscal years beginning after September 15, 2012, with early adoption permitted. The Company believes the adoption of this standard will not have a material impact on its consolidated financial statements.

In December 2011, an Accounting Standards Update was issued that requires disclosure of information about offsetting and related arrangements to enable users of the Company’s consolidated financial statements to understand the effect of those arrangements on the Company’s financial position. The new guidance is effective for annual reporting periods beginning on or after January 1, 2013, and interim periods within those annual periods. The disclosures required are to be applied retrospectively for all comparative periods presented. Upon adoption, the Company does not expect that this standard will materially impact our disclosures included in our consolidated financial statements.

3. Beneficial Conversion Charge ("BCC")

When issuing debt or equity securities that are convertible into common stock at a discount from the fair value of the common stock at the date the debt or equity financing is committed, the Company is required to record a BCC in accordance with Accounting Standards Codification ("ASC") 470-20. This BCC is measured as the difference between the fair values of the securities at the time of issue and the fair value of the common stock at the commitment date.

In 2011, a non-cash BCC of $9.2 million was recorded when the Series B Preferred Stock was converted into common stock. The BCC represents a $1.00 per share discount on the fair value of our common stock. The carrying value of the preferred stock was based on its fair value at issuance, which was estimated using the common stock price reduced for a lack of marketability between the issuance date and the anticipated date of conversion.

4. Accrued Expenses

Accrued expenses consist of the following:

	As of December 31,	
	2012	2011
	(in thousands)	
Accrued clinical trial expenses	$ 1,460	$ 675
Liability for stock-based compensation awards	1,204	-
Accrued professional fees	185	110
Accrued interest payable	80	-
Other accrued expenses	4	15
	$ 2,933	$ 800

5. Business Combination

The Company entered into an Agreement and Plan of Merger with Transave, Inc. on December 1, 2010. The Merger was accounted for using the acquisition method of accounting and, accordingly, the tangible and intangible assets acquired (including in-process research and development and goodwill) and liabilities assumed were recorded at their estimated fair values as of the date of the acquisition. Transaction costs related to the Merger were $6.0 million of which $4.8 million was expensed in 2010 and $1.2 million was expensed in 2009. These costs were included in general and administrative expenses in the Consolidated Statements of Comprehensive Loss.

The following unaudited pro forma financial information combines the consolidated results of operations as if the Merger had occurred as of the beginning of the period presented.

	2010
	(in thousands)
Revenues	$ 7,654
Operating loss	$ (20,266)
Net loss after income taxes	$ (25,873)

6. Identifiable Intangible Assets and Goodwill

In 2011, the Company recorded a non-cash impairment loss of $26.0 million related to the impairment of in-process research and development and goodwill. The impairment resulted from the fact that in August 2011, subsequent to our phase 2 trials and prior to starting a phase 3 trial, the Company announced that the FDA placed a clinical hold on its phase 3 clinical trials for ARIKACE in CF patients with *Pseudomonas* lung infections and in patients with NTM lung infections. A clinical hold is a notification issued by the FDA to the sponsor to delay a proposed clinical trial or suspend an ongoing clinical trial. The clinical holds were subsequently lifted in the first half of 2012.

The Company's management determined the clinical hold was an indicator of possible impairment of in-process research and development and goodwill assets due to the associated additional costs, and, therefore, interim impairment testing was performed as of September 30, 2011. Using the income approach the impairment analysis compared the fair value of the in-process research and development intangible assets with their respective carrying amounts. 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. Additionally, the carrying value of the business exceeded its fair value, and accordingly we performed the second step of the impairment test by comparing the carrying value of goodwill to its implied fair value. The impairment review resulted in impairment losses for both assets. Non-cash charges of $19.7 million and $6.3 million were recognized for the decline in the fair value of in-process research and development and goodwill assets, respectively, as of September 30, 2011. The non-cash charge of $26.0 million was recorded as an impairment loss and classified as an operating expense in the Consolidated Statements of Comprehensive Loss.

We believe there are no indicators of impairment of the Company's in-process research and development intangible assets as of December 31, 2012.

7. 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, 2012	2011
		(in thousands)	
Lab equipment	7	$ 3,197	$ 3,072
Furniture and fixtures	7	65	56
Computer hardware and software	3-5	588	469
Office equipment	7	117	115
Leasehold improvements	lease term	581	577
		4,548	4,289
Less accumulated depreciation and amortization		(2,882)	(2,352)
Fixed assets, net		$ 1,666	$ 1,937

Depreciation and amortization expense was $0.6 million, $0.3 million and $0.1 million for the years ended December 31, 2012, 2011 and 2010, respectively. Depreciation expense includes depreciation for equipment under capital lease obligations.

Fixed assets include equipment held under capital lease obligations with an approximate net carrying value of $0.3 million and $0.4 million as of December 31, 2012 and 2011, respectively.

Certain owned lab equipment totaling $0.3 million that is used in the manufacturing process of the Company's drug supply is located at its contract manufacturer.

8. *Debt*

On June 29, 2012, the Company and its domestic subsidiaries, as co-borrowers, entered into a Loan and Security Agreement that allowed the Company to borrow up $20.0 million in $10.0 million increments ("Loan Agreement"). The Company borrowed the first and second $10.0 million increments by signing two Secured Promissory Notes ("Notes A and B") on June 29, 2012 and December 27, 2012, respectively. Notes A and B bear interest at 9.25%. Note A is to be repaid over a 42-month period with the first twelve monthly payments representing interest only followed by thirty monthly equal payments of principal and interest. Note B is to be repaid over a 36-month period with the first six monthly payments representing interest only followed by thirty monthly equal payments of principal and interest. The interest only period is extendable to December 31, 2013, contingent upon completion of certain ARIKACE-related development milestones. The principal monthly repayments for Notes A and B are scheduled to begin on August 1, 2013 and end on January 1, 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. Debt issuance fees paid to the lender were recorded as a discount on the 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 Loan Agreement, 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. 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, 2012.

	December 31, 2012 (in thousands)
Debt:	
Notes payable	$ 20,000
Add:	
Accretion of end of term charge	44
Less:	
Issuance fees paid to lender	(194)
Discount from warrant	(622)
Current portion of long-term debt	(3,007)
Long-term debt	$ 16,221

Future principal repayments of the two Notes are as follows (in thousands):

Year Ending December 31:		
2013	$	3,007
2014		7,724
2015		8,481
2016		788
Total	$	20,000

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. We believe the estimated fair value at December 31, 2012 approximates the carrying amount.

9. Stockholders' Equity

Common Stock – As of December 31, 2012, the Company had 500,000,000 shares of common stock authorized with a par value of $0.01 and the Company had reserved 1,817,839 shares of common stock for issuance upon the exercise of outstanding common stock options, 215,525 for issuance upon the vesting of restricted stock units, and 329,932 shares of common stock for issuance upon the exercise of the outstanding warrant.

On September 28, 2012, we completed a registered direct public offering of 6,304,102 shares of our Common Stock to certain investors at a price of $4.07 per share, resulting in proceeds of $25.7 million.

Warrant - In conjunction with entering into the Loan Agreement (See Note 8 – 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 is being amortized to interest expense over the term of the related debt using the effective interest method. This warrant expires on June 29, 2017.

10. Stock-Based Compensation

The Company has two equity compensation plans; 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.

Under the terms of the 2000 Stock Incentive Plan, the Company is authorized to grant a variety of incentive awards based on our common stock, including stock options (both incentive options and non-qualified options), performance shares and other stock awards to all employees and non-employee directors. At the 2011 Annual Meeting of Shareholders held on May 18, 2011, the Company's shareholders approved an amendment to increase the number of authorized shares under this plan by 3,000,000 shares. As of December 31, 2012, the 2000 Stock Incentive Plan provides for the issuance of a maximum of 3,925,000 shares of common stock and also includes per person annual sub-limits for the issuance of a maximum of 75,000 stock options, 12,500 performance shares (including RSUs) and 12,500 shares of restricted stock. As of December 31, 2012, 737,448 shares of the Company's common stock were reserved for future grants (or issuances) of restricted stock, restricted stock units, stock options, and stock warrants under the 2000 Stock Incentive Plan.

Under the terms of the Stock Purchase Plan, eligible employees have the opportunity to purchase our common stock at a discount. An option gives its holder the right to purchase shares of our common stock, up to a maximum value of $25,000 per year. The Stock Purchase Plan provides for the issuance of a maximum of 150,000 shares of our common stock to participating employees. The Company did not offer employees the right to purchase common stock under the Stock Purchase Plan during 2012, 2011 or 2010. As of December 31, 2012, 150,000 shares of the Company's common stock were reserved for future issuances of common stock under the Stock Purchase Plan.

Stock Options - The Company calculates the fair value of stock options granted using the Black-Scholes valuation model. The Company calculates the fair value of stock options granted outside of the 2000 Stock Incentive Plan using liability accounting. These awards are classified as a liability and remeasured at fair value at the end of each reporting period using the Black-Scholes valuation model and changes in fair value are 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 stock options granted under and outside the 2000 Stock Incentive Plan during the years ended December 31, 2012 and 2011 (no stock options were granted during 2010).

	2012	2011
Volatility	96.2%	111.6%
Risk-free interest rate	0.7%	0.9%
Dividend yield	0.0%	0.0%
Expected option term (in years)	6.25	6.25
Weighted-average grant date fair value of stock options granted	$ 3.21	$ 2.68

For the year ended December 31, 2012 and 2011, 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 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 is the basis for future forfeiture expectations.

The following table summarizes stock option activity for stock options granted under and outside the 2000 Stock Incentive Plan for the years ended December 31, 2012, 2011 and 2010 as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value
Options outstanding at December 31, 2009	259,275	$ 23.00		
Granted	-	-		
Exercised	-	-		
Forfeited and expired	(45,000)	48.04		
Options outstanding at December 31, 2010	214,275	$ 18.43		
Vested and expected to vest at December 31, 2010	214,275	$ 18.43		
Exercisable at December 31, 2010	214,275	$ 18.43		
Options outstanding at December 31, 2010	214,275	$ 18.43		
Granted	766,000	3.77		
Exercised	(5,200)	6.16		
Forfeited and expired	(83,324)	26.57		
Options outstanding at December 31, 2011	891,751	5.15		
Vested and expected to vest at December 31, 2011	816,414	5.30		
Exercisable at December 31, 2011	125,751	13.54		
Options outstanding at December 31, 2011	891,751	$ 5.15		
Granted	1,116,384	4.12		
Exercised	(30,250)	7.08		
Forfeited and expired	(160,046)	9.54		
Options outstanding at December 31, 2012	1,817,839	4.10	7.84	$ 4,790,817
Vested and expected to vest at December 31, 2012	1,692,915	4.11	7.71	$ 4,457,650
Exercisable at December 31, 2012	438,145	4.59	2.43	$ 1,003,740

The total intrinsic value of stock options exercised during the years ended December 31, 2012 and 2011 were $24,590 and $23,482, respectively. The Company recognized stock-based compensation expense related to stock options of approximately $1.8 million, $0.3 million $0.4 million for the years ended December 31, 2012, 2011 and 2010, respectively. Stock-based compensation expense during 2012 includes $0.5 million of expense resulting from modifications made to stock options held by certain employees that were terminated during 2012. General and administrative expenses include $1.5 million, $0.2 million and $0.0 million and research and development expenses include $0.3 million, $0.1 million and $0.0 million of stock-based compensation expense in the Consolidated Statement of Comprehensive Loss for the years December 31, 2012, 2011 and 2010, respectively. As of December 31, 2012, there was $5.9 million of unrecognized compensation expense related to unvested stock options, which is expected to be recognized over a weighted average period of 3.56 years.

Outstanding as of December 31, 2012					Exercisable as of December 31, 2012	
Range of Exercise Prices		Number of Options	Weighted Average Remaining Contractual Term (in Years)	Weighted Average Excersise Price	Number of Options	Weighted Average Excersise Price
$ 3.03	$ 3.13	482,305	6.35	$ 3.03	234,495	$ 3.03
$ 3.14	$ 3.39	21,400	9.44	$ 3.24	-	$ -
$ 3.40	$ 3.47	708,314	9.69	$ 3.40	-	$ -
$ 3.48	$ 4.05	16,500	9.51	$ 3.69	-	$ -
$ 4.55	$ 4.96	186,170	9.74	$ 4.55	-	$ -
$ 4.97	$ 5.89	4,000	9.75	$ 4.97	-	$ -
$ 5.90	$ 6.33	198,400	1.66	$ 5.90	182,900	$ 5.90
$ 6.34	$ 8.29	185,250	9.64	$ 6.64	5,250	$ 6.50
$ 8.30	$ 17.59	10,250	0.80	$ 9.18	10,250	$ 9.18
$ 17.60	$ 17.60	5,250	0.36	$ 17.60	5,250	$ 17.60

Restricted Stock and Restricted Stock Units – The Company grants Restricted Stock ("RS") and Restricted Stock Units ("RSUs") to eligible employees, including our executives. 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 under the Company's 2000 Stock Incentive Plan are generally valued at the market price of the Company's common stock on the date of grant. In the first quarter of 2011, the Company granted RSUs outside of the 2000 Stock Incentive Plan and those awards were accounted for as a liability as they would have been deemed to be cash settled until additional shares were authorized for issuance under the 2000 Stock Incentive Plan. In May 2011, additional shares under the 2000 Stock Incentive Plan were authorized and the RSUs were converted to equity awards and were valued at the market price of our common stock on that date. In addition, RSUs granted in excess of certain plan sub-limits are considered to be granted outside the 2000 Stock Incentive Plan and are classified as a liability and remeasured at fair value at the end of each reporting period and changes in fair value are included in compensation expense in the Consolidated Statements of Comprehensive Loss (see additional disclosures related to RSUs granted outside the 2000 Stock Incentive Plan at the end of this footnote). 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, which is generally three years.

The following table summarizes the total RS and RSU awards granted both under and outside of the 2000 Stock Incentive Plan during the years ended December 31, 2012, 2011 and 2010:

	Number of RS	Weighted Average Grant Price	Number of RSU's	Weighted Average Grant Price
Outstanding at December 31, 2009	8,772	$ 17.10	-	-
Granted	30,270	8.80	-	-
Released	(39,042)	10.72	-	-
Outstanding at December 31, 2010	-	-	-	-
Granted	-	-	491,255	$ 6.36
Forfeited	-	-	(4,230)	5.13
Outstanding at December 31, 2011	-	-	487,025	6.37
Granted	-	-	61,011	3.44
Released			(322,819)	4.59
Forfeited	-	-	(9,692)	5.69
Outstanding at December 31, 2012	-	$ -	215,525	$ 6.26
Expected to Vest	-	$ -	206,395	$ 6.23

The Company recognized stock-based compensation expense related to RS and RSUs of approximately $1.2 million, $1.3 million and $0.3 million for the years ended December 31, 2012, 2011 and 2010, respectively. Stock-based compensation expense during 2012 includes $1.2 million of expense resulting from modifications made to RSUs held by certain employees that were terminated during 2012. General and administrative expenses include $0.8 million, $0.9 million and $0.2 million and research and development expenses include $0.4 million, $0.4 million and $0.1 million of stock-based compensation expense in the Consolidated Statements of Comprehensive Loss for the years ended December 31, 2012, 2011 and 2010, respectively. As of December 31, 2012, there was $ 0. 5 million of unrecognized compensation expense related to unvested RSUs, which is expected to be recognized over a weighted average period of 0.9 years. The total fair value of the RSUs and RS that vested during 2012 and 2011 was $1.5 million and $0.4 million, respectively.

Awards Granted Outside of the 2000 Stock Incentive Plan - In connection with a recent review of equity compensation awards made under the 2000 Stock Incentive Plan, the Company determined that it had inadvertently exceeded the annual per-person sub-limits in connection with awards previously made to certain of its current and past officers and directors. The aggregate amount of common stock represented by these awards in excess of the per person annual sub-limits during the two years ended December 31, 2012, which consisted of RSUs and stock options, is approximately 1.4 million shares. Such awards are included in the stock option and RS and RSU tables and related disclosures above. The awards that exceeded the per person sub-limits included certain awards issued immediately following the Company's business combination with Transave, awards negotiated with new hires pursuant to employment agreements or offers of employment, and certain other awards made subsequent to the Company's 2011 one-for-ten reverse stock split. 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 and recorded a liability of $1.2 million which is included in Accrued expenses as of December 31, 2012.

11. Income Taxes

The provision for income taxes was $0 during the years ended December 31, 2012 and 2011, and $78,000 during the year ended December 31, 2010. The Company's effective tax rate was 0.0% during the years ended December 31, 2012 and 2011, and (1.0%) in the year ended December 31, 2010. The Company is subject to US federal and state income taxes. The Company has never been audited and the statute of limitations for tax audit is generally open for the years 2009 and later. However, except in 2009, the Company has incurred net operating losses since inception. 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, 2012 and 2011, 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 anticipate any material changes in the amount of unrecognized tax positions over the next twelve months.

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

	Years Ended December 31,		
	2012	2011	2010
Statutory federal tax rate	34%	34%	34%
Permanent items	-	(4%)	(9%)
State income taxes, net of federal benefit	4%	3%	1%
Research and development credit	1%	5%	-
Expired net operating loss carryforwards	(15%)	(10%)	-
Alternative minimum tax	-	-	1%
Change in valuation allowance	(22%)	(27%)	(28%)
Other	(2%)	(1%)	-
Effective tax rate	0%	0%	(1)%

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,	
	2012	2011
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 128,257	$ 119,719
General business credits	10,501	10,324
Alternative Minimum Tax (AMT) credit	418	418
Other	3,007	1,791
Gross deferred tax assets	$ 142,183	$ 132,252
Deferred tax liabilities:		
In-process research and development	$ (22,093)	$ (22,093)
Other	-	(170)
Deferred tax liabilities	$ (22,093)	$ (22,263)
Net deferred tax assets	$ 120,090	$ 109,989
Valuation Allowance	(120,090)	(109,989)
Net deferred tax assets	$ -	$ -

The net deferred tax assets (prior to applying the valuation allowance) of $120.1 million and $110.0 million at December 31, 2012 and 2011, 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 $10.1 million as it is more likely than not that such tax benefits will not be realized.

At December 31, 2012, the Company had net operating loss carryforwards for income tax purposes of approximately $350.0 million available to offset future taxable income, if any. The NOL carryovers and general business tax credits expire in various years beginning in 2013.

Utilization of the NOLs and general business tax credits carryforwards may be subject to a substantial limitation under Section 382 of the Internal Revenue Code of 1986 due to changes in ownership of the Company that have occurred previously or that could occur in the future. These ownership changes may limit the amount of NOL and general business tax credits carryforwards that can be utilized annually to offset future taxable income and tax, respectively. 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 stockholders' subsequent disposition of those shares, may have resulted in a change of control, as defined by Section 382, and it issued a substantial amount of shares of common stock as part of its merger with Transave, Inc. in December 2010. Due to the significant complexity and cost associated with a change in control study, and because there could be additional changes in control in the future, the Company has not yet formally assessed whether there has been one or more changes in control since the Company's formation. If the Company has experienced a change of control at any time since Company formation, utilization of its NOL or general business tax credit carryforwards would be subject to the limitation rules under Section 382. Any limitation may result in expiration of a portion of the NOL or general business tax credit carryforwards before utilization which would reduce the Company's gross deferred tax assets.

12. License and Collaboration Agreements

In-License Agreements

Ipsen and Genentech - In March 2007, the Company was 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. In November 2008, the Company gained Royalty-Free Worldwide Rights for IPLEX from Ipsen and Genentech in connection with potential expanded access ALS programs.

PARI Pharma GmbH - In April 2008, the Company entered into a licensing agreement with PARI Pharma GmbH for use of the optimized eFlow Nebulizer System for delivery of ARIKACE in treating patients with CF, bronchiectasis, and NTM infections. Insmed has rights to several US and foreign issued patents and patent applications involving improvements to the optimized eFlow Nebulizer System. In consideration of this agreement, PARI shall 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 ARIKACE and the device, first receipt of marketing approval in the US for ARIKACE and the device, and first receipt of marketing approval in a major EU country for ARIKACE. In addition, PARI will receive royalty payments on commercial sales of ARIKACE.

Out-License Agreements

NAPO Pharmaceuticals - In January 2007, the Company entered into an agreement with NAPO Pharmaceuticals, whereby it granted NAPO a license for INSM-18 also known as Masoprocal. The license gives NAPO the right to develop, manufacture and commercialize Masoprocal products for any indications relating specifically to diabetes, cardiac disease, vascular disease, metabolic disease and Syndrome X. The agreement calls for payments from NAPO to the Company upon the achievement of certain milestones which have not yet been met.

TriAct - In December, 2010, the Company entered into an agreement with TriAct Therapeutics Inc. ("TriAct") whereby it granted TriAct an exclusive license for INS-18 also known as Masoprocal. The license gives TriAct the right to develop, manufacture and commercialize Masoprocal products for any indications relating specifically to oncology. The agreement calls for the issue of TriAct common stock to Insmed upon the achievement of certain milestones. To date, no milestones have been achieved and no common stock has been received.

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 Holdings AB and Premacure AB of Sweden (collectively, "Premacure") 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 (the "Premacure License Agreement"). In March 2013, we amended the Premacure License Agreement to provide Premacure with the option, exercisable by Premacure any time prior to April 30, 2013, to pay us $11.5 million and assume any of our royalty obligations to other parties in exchange for a fully paid license. If Premacure exercises this option, we would not be entitled to future royalties from Premacure.

Collaboration Agreements

Cystic Fibrosis Foundation Therapeutics, Inc. - In 2005 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 ARIKACE product. If ARIKACE 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 sales milestones are met within 5 years of the drug commercialization approval in the US, the Company would owe an additional payment of $3.9 million. Since there is significant development risk associated with ARIKACE, we have not accrued these obligations.

National Institutes of Allergy and Infectious Diseases - In 2009 and 2012, we entered into a cooperative research and development agreement (CRADA) with National Institutes of Allergy and Infectious Diseases (NIAID) to design and conduct our phase 2 study of ARIKACE in patients with NTM. NIAID has also agreed to provide biostatistical advisory input in connection with the phase 2 NTM study. If we decide not to continue with the commercialization of ARIKACE in NTM, NIAID will have the right to complete the clinical trial. Further, NIAID may elect to pursue its rights to obtain license rights to certain inventions made under the CRADA.

13. Commitments and Contingencies

Commitments

The Company has two operating leases for office and laboratory space located in Monmouth Junction, NJ through December 31, 2014. Future minimum rental payments under these two leases total approximately $1.4 million. We continue to lease 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 $1.9 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. The remaining accrual for this charge was $0.9 million as of December 31, 2012.

Rent expense charged to operations was $1.0 million, $1.0 million and $0.5 million for the years ended December 31, 2012, 2011 and 2010, respectively. Future minimum rental payments required under the Company's operating leases are as follows (in thousands).

Year Ending December 31:		
2013	$	1,188
2014		1,201
2015		498
2016		425
Total	$	3,312

Legal Proceedings

Cacchillo v. Insmed

On October 6, 2010, a complaint was filed against the Company by Angeline Cacchillo ("Plaintiff") in the U.S. District Court for the Northern District of New York (the "Court"), captioned *Cacchillo v. Insmed, Inc.* , No. 1:10-cv-0199, seeking monetary damages and a court order requiring Insmed to support Plaintiff's compassionate use application to the FDA and if approved, to provide Plaintiff with IPLEX. Plaintiff was a participant in the phase II clinical trial of IPLEX sponsored by us evaluating the effectiveness of the investigational drug in patients with type 1 myotonic muscular dystrophy ("MMD"). In the complaint, Plaintiff alleged (i) violation of constitutional due process and equal protection by depriving Plaintiff of continued access to IPLEX, (ii) fraudulent inducement to enter the phase II clinical trial with the false promise to support Plaintiff's compassionate use application to the FDA, (iii) negligent representation that the Company would support Plaintiff's compassionate use application, (iv) breach of contract, seeking monetary and non-monetary damages, (v) intentional infliction of emotional distress by refusing to support Plaintiff's compassionate use application after providing IPLEX, (vi) violation of an assumed duty of care to Plaintiff, (vii) breach of fiduciary duty to Plaintiff, (viii) negligence and (ix) unjust enrichment. Plaintiff seeks compensatory and punitive monetary damages and sought injunction relief as noted above.

On October 7, 2010, Plaintiff filed a motion for a preliminary injunction that would require us to provide a written statement supporting the "compassionate use" of IPLEX for Plaintiff and directing us to provide IPLEX to Plaintiff at cost in the event that the compassionate use application were granted by the FDA. On October 22, 2010, the Court denied Plaintiff's motion for the preliminary injunction concluding that the Court lacked subject matter jurisdiction with respect to her claim for a preliminary injunction. Plaintiff appealed the Court's denial of her motion for a preliminary injunction to the U.S. Court of Appeals for the Second Circuit, which affirmed the trial court's order denying the Plaintiff's motion for a preliminary injunction.

We filed a motion with the Court to dismiss all of the outstanding claims, and on June 29, 2011, the Court dismissed six of Plaintiff's claims, leaving outstanding the claims for (i) fraudulent inducement, (ii) negligent misrepresentation, and (iii) breach of contract. The Company filed an answer and affirmative defenses with the Court on July 12, 2011. Plaintiff's claim for monetary damages with respect to these claims remains outstanding. The parties completed discovery on or about June 1, 2012. The Company filed a Motion for Summary Judgment on August 1, 2012 seeking judgment in our favor on the three claims remaining in the case and the motion was fully submitted on October 9, 2012. On January 19, 2013, the Court granted the Company's Motion for Summary Judgment and dismissed all of the outstanding claims. Plaintiff filed a Notice of Appeal on March 15, 2013. The Company expects that the parties will submit briefs before the end of 2013, with a decision expected sometime in the first half of 2014.

Pilkiewicz v. Transave LLC

On March 28, 2011, Frank G. Pilkiewicz and other former stockholders of Transave (collectively, the "Petitioners") filed an appraisal action against the Company's subsidiary Transave, LLC in the Delaware Court of Chancery captioned *Frank G. Pilkiewicz, et al. v. Transave, LLC* , C.A. No. 6319-CS. On December 13, 2011, following the mailing of the revised notice of appraisal rights in accordance with the settlement terms of *Mackinson et al. v. Insmed* , an Amended Petition for Appraisal of Stock was filed by the Petitioners.

The Petitioners seek appraisal under Delaware law of their total combined common stock holdings representing total dissenting shares of approximately 7.77 million shares of Transave, Inc. common stock (the "Transave Stock"). The Petitioners are challenging the value of the consideration that they would be entitled to receive for their Transave Stock under the terms of the merger.

Under the terms of the merger agreement, certain of the former stockholders of Transave (the "Transave Stockholders") are obligated to indemnify the Company for certain liabilities in connection with the appraisal action. The Company notified the Transave Stockholders in May 2012 that the Company is seeking indemnification in accordance with the merger agreement and that it will continue to retain the aggregate amount of the holdback shares totaling 1.76 million shares, as security for any indemnification payments due under the merger agreement. Discovery is ongoing and the trial is scheduled to begin September 30, 2013. The Company believes that the allegations contained in the amended petition are without merit and we intend to continue to vigorously defend this action. It is not possible at this time to estimate the amount of loss or range of possible loss, if any, that might result from an adverse resolution of this action.

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 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 the Company's consolidated financial position, results of operations or cash flows.

14. Quarterly Financial Data (Unaudited)

The following table summarizes unaudited quarterly financial data for the years ended December 31, 2012 and 2011 (in thousands, except per share data).

	2012				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Revenues	$ -	$ -	$ -	$ -	$ -
Operating loss	(7,264)	(9,983)	(9,353)	(15,838)	(42,438)
Net loss after income taxes	(6,845)	(9,696)	(9,382)	(15,451)	(41,374)
Basic and diluted net loss attributable to common stockholders per common share	$ (0.28)	$ (0.39)	$ (0.38)	$ (0.49)	$ (1.56)

	2011				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
Revenues	$ 1,601	$ 978	$ 435	$ 1,403	$ 4,417
Operating loss	(7,415)	(10,473)	(34,960)	(8,871)	(61,719)
Net loss after income taxes	(6,894)	(10,017)	(34,591)	(8,162)	(59,664)
Basic and diluted net income (loss) attributable to common stockholders per common share	$ (0.85)	$ (0.40)	$ (1.39)	$ (0.33)	$ (2.95)

Basic and diluted net income (loss) per share amounts included in the above tables are 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.

15. Subsequent Events

In connection with a recent review by the Company of equity compensation awards made under its 2000 Stock Incentive Plan, which is described in greater detail in Footnote 10 herein, the Company determined that it had inadvertently exceeded the annual per-person sub-limits set forth in the 2000 Stock Incentive Plan. The awards that exceeded the per-person sub-limits included certain RS, RSU and stock option awards made to certain of its current and past officers and directors. The amount of common stock represented by these awards in excess of the per-person annual sub-limits totaled approximately 1.6 million shares. The awards that exceeded the per-person sub-limits included several awards that were issued immediately following the Company's business combination with Transave, several awards that were negotiated with new hires pursuant to employment agreements or offers of employment, and certain other awards made subsequent to our 2011 one-for-ten reverse stock split. The Company has not exceeded the aggregate maximum share limit approved by shareholders under the 2000 Stock Incentive Plan (currently 3,925,000 shares of common stock), whether as a result of previously-issued awards or currently outstanding awards.

As a result of the foregoing review and findings with respect to awards in excess of the per-person annual sub-limits, on March 7, 2013, the Company's Board approved a remediation and compliance plan recommended by a special committee of the Board. Pursuant to the remediation and compliance plan, on March 14, 2013, the Company provided notice to each current employee and director who was a recipient of an affected equity compensation award. As of March 15, 2013, each current employee and director who holds an affected equity compensation award that is currently unvested and/or unexercised, has entered into a waiver and consent with the Company. Pursuant to such waiver and consent, each affected current employee or director agreed that the unvested portion of such awards in excess of the sub-limits shall not vest and shall not become exercisable and any vested portion of such awards of stock options in excess of the sub-limits shall not be exercisable, in each case, unless the Company's shareholders ratify and approve the portion of the affected awards that were in excess of the applicable sub-limits. If the Company's shareholders do not ratify and approve the affected portion of such awards, such portions would be deemed forfeited. In furtherance of the foregoing, on March 7, 2013, as part of the remediation and compliance plan, the Board approved the recommendation of a special committee of the Board that we seek shareholder approval at the Company's 2013 annual meeting of shareholders to ratify and approve the excess portions of the affected awards.

On March 12, 2013, the Company notified Nasdaq of the grants previously made in excess of the annual per-person sublimits provided for by 2000 Stock Incentive Plan. The Company believes that a decision by the Company to increase the annual sub-limits would have constituted an immaterial amendment to the 2000 Stock Incentive Plan, which amendment would not have required shareholder approval under applicable Nasdaq guidance. However, because the grant of certain awards exceeded the sublimits applicable at the time the grants were made, it is possible that Nasdaq will conclude that the Company issued securities pursuant to the 2000 Stock Incentive Plan without shareholder approval in violation of Nasdaq Listing Rule 5635(c).

In a March 13, 2013 letter to Nasdaq, the Company submitted a remediation and compliance plan, which the Company refers to as the remediation plan, to address the grants made in excess of the 2000 Stock Incentive Plan sub-limits. Among other items, the Company's remediation plan conditions the continued vesting and exercise of the portion of each equity compensation award issued to our current employees and directors in excess of the 2000 Stock Incentive Plan's sub-limits on approval by the Company's shareholders of such portion of the affected grants. If our shareholders do not ratify and approve the affected portions of such awards, such portions would be deemed forfeited.

As part of the Company's remediation plan, and after receiving confirmation from Nasdaq's staff on Nasdaq's continued reliance on Staff Interpretation Letter 2007-28, on March 15, 2013, the compensation committee of the Board recommended and the Board approved an amendment to the 2000 Stock Incentive Plan to replace the three individual annual per person equity compensation limits with a single annual aggregate stock option, performance share and restricted stock sub-limit of 1,500,000 shares. The Company did not change the overall share reserve for the 2000 Stock Incentive Plan of 3,925,000 shares, which was approved by the Company's shareholders in May 2011.

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 (previously filed as Exhibit 2.1 to Insmed Incorporated's Current Report on Form 8-K filed on December 2, 2010 and incorporated herein by reference).
3.1	Articles of Incorporation of Insmed Incorporated, as amended through June 14, 2012 (filed herewith).
3.2	Amended and Restated Bylaws of Insmed Incorporated (incorporated by reference from Exhibit 3.1 to Insmed Incorporated's Current Report on Form 8-K filed on March 9, 2012).
4.1	Specimen stock certificate representing common stock, $0.01 par value per share, of the Registrant (previously filed as Exhibit 4.2 to Insmed Incorporated's Registration Statement on Form S-4/A (Registration No. 333-30098)).
4.2	Shareholders Agreement, dated December 1, 2010, among Insmed Incorporated and each of the listed shareholders (incorporated by reference from Exhibit 4.1 to Insmed Incorporated's Current Report on Form 8-K filed on December 2, 2010).
4.3	Registration Rights Agreement, dated December 1, 2010, among Insmed Incorporated and each of the listed shareholders (incorporated by reference from Exhibit 4.2 to Insmed Incorporated's Current Report on Form 8-K filed on December 2, 2010).
4.4	Warrant Agreement to purchase shares of common stock issued to Hercules Technology Growth Capital, Inc., dated as of June 29, 2012 (incorporated by reference from Exhibit 4.1 to Insmed Incorporated's Current Report on Form 8-K filed on July 2, 2012.
10.1**	Amended and Restated 2000 Employee Stock Purchase Plan (incorporated by reference from Exhibit 10.22 to Insmed Incorporated's Annual Report on Form 10-K for the year ended December 31, 2006).
10.2**	Amended and Restated 2000 Stock Incentive Plan (incorporated by reference from Exhibit A to Amendment 1 to Insmed Incorporated's Definitive Proxy Statement filed on April 20, 2011).
10.3**	Form of Award Agreement for Restricted Stock Units issued to employees pursuant to Insmed's Amended and Restated 2000 Stock Incentive Plan (filed herewith).
10.4**	Form of Award Agreement for Restricted Stock Units issued to directors pursuant to Insmed's Amended and Restated 2000 Stock Incentive Plan (filed herewith).
10.5**	Form of Award Agreement for an Incentive Stock Option pursuant to Insmed's Amended and Restated 2000 Stock Incentive Plan (filed herewith).
10.6**	Form of Award Agreement for a Non-Qualified Stock Option pursuant to Insmed's Amended and Restated 2000 Stock Incentive Plan (filed herewith).
10.7**	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).
10.8**	Employment Agreement, effective as of July 18, 2011, between Insmed Incorporated and Andrea Holtzman Drucker (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on July 18, 2011).

10.9**	Employment Agreement, effective as of May 14, 2012, between Insmed Incorporated and Donald Hayden, Jr. (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on May 17, 2012).
10.10**	Letter Agreement, dated September 10, 2012, between Insmed Incorporated and Donald Hayden, Jr. (incorporated by reference from Exhibit 10.3 to Insmed Incorporated's Current Report on Form 8-K filed on September 11, 2012).
10.11**	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).
10.12**	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).
10.13**	Employment Agreement, dated December 2, 2010, between Insmed Incorporated and Nicholas Labella, Jr. (incorporated by reference from Exhibit 10.3 to Insmed Incorporated's Current Report on Form 8-K filed on February 1, 2011).
10.14**	Separation and Release Agreement, dated October 5, 2012, between Insmed Incorporated and Nicholas Labella (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on October 5, 2012).
10.15**	Employment Agreement, dated December 2, 2010, between Insmed Incorporated and Kevin P. Tully (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Current Report on Form 8-K filed on February 1, 2011).
10.16**	Separation and Release Agreement, effective as of July 26, 2012, between Insmed Incorporated and Kevin Tully (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on July 30, 2012).
10.17**	Employment Agreement, dated December 2, 2010, between Insmed Incorporated and Timothy Whitten (incorporated by reference from Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on February 1, 2011).
10.18**	Severance Agreement, dated September 10, 2012, between Insmed Incorporated and Timothy Whitten (incorporated by reference from Exhibit 10.2 to Insmed Incorporated's Current Report on Form 8-K filed on September 11, 2012).
10.19	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).
10.20*	Settlement, license and development agreement, dated March 5, 2007, between Insmed Incorporated, Insmed Therapeutic Proteins, Inc., Celtrix Pharmaceuticals, Tercica Inc., and Genentech, Inc. (previously filed as Exhibit 10.1 to Insmed's Quarterly Report on 10-Q filed on May 10, 2007, and incorporated herein by reference).
10.21	Asset Purchase Agreement, dated February 12, 2009, between Protein Transaction LLC (a wholly owned subsidiary of Merck & Co. Inc.) Insmed Incorporated and Merck & Co., Inc. (previously filed as Exhibit 10.1 to Insmed Incorporated's Current Report on Form 8-K filed on February 13, 2009 and incorporated herein by reference).

10.22*	License agreement dated April 25, 2008, between Transave, Inc. and PARI Pharma GmbH (filed herewith).
21.1	Subsidiaries of Insmed Incorporated (filed herewith).
23.1	Consent of Ernst & Young LLP
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.
31.2	Certification of William H. Lewis, Chief Executive Officer of Insmed Incorporated, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2003.
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.
32.2	Certification of Andrew T. Drechsler, Chief Financial Officer (Principal Financial and Accounting Officer) of Insmed Incorporated, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2003.

+ 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 3.1

ARTICLES OF INCORPORATION
of
INSMED, INC.

ARTICLE I

The name of the Corporation shall be Insmed, Inc.

ARTICLE II

The purpose for which the Corporation is formed is to transact any or all lawful business, not required to be specifically stated in these Articles of Incorporation, for which corporations may be incorporated under the Virginia Stock Corporation Act, as amended from time to time, and any legislation succeeding thereto (the "VSCA").

ARTICLE III

The aggregate number of shares that the Corporation shall have authority to issue shall be 200,000,000 shares of Preferred Stock, par value $.01 per share (hereinafter called "Preferred Stock"), and 500,000,000 shares of Common Stock, par value $.01 per share (hereinafter called "Common Stock"). The following is a description of each of such classes of stock, and a statement of the preferences, limitations, voting rights and relative rights in respect of the shares of each such class:

1. Authority to Fix Rights of Preferred Stock . The Board of Directors shall have authority, by resolution or resolutions, at any time and from time to time to divide and establish any or all of the unissued shares of Preferred Stock not then allocated to any series of Preferred Stock into one or more series, and, without limiting the generality of the foregoing, to fix and determine the designation of each such series, the number of shares that shall constitute such series and the following relative rights and preferences of the shares of each series so established:

(a) The annual or other periodic dividend rate payable on shares of such series, the time of payment thereof, whether such dividends shall be cumulative or non-cumulative, and the date or dates from which any cumulative dividends shall commence to accrue;

(b) the price or prices at which and the terms and conditions, if any, on which shares of such series may be redeemed;

(c) the amounts payable upon shares of such series in the event of the voluntary or involuntary dissolution, liquidation or winding-up of the affairs of the Corporation;

(d) the sinking fund provisions, if any, for the redemption or purchase of shares of such series;

(e) the extent of the voting powers, if any, of the shares of such series;

(f) the terms and conditions, if any, on which shares of such series may be converted into shares of stock of the Corporation of any other class or classes or into shares of any other series of the same or any other class or classes;

(g) whether, and if so the extent to which, shares of such series may participate with the Common Stock in any dividends in excess of the preferential dividend fixed for shares of such series or in any distribution of the assets of the Corporation, upon a liquidation, dissolution or winding-up thereof, in excess of the preferential amount fixed for shares of such series; and

(h) any other preferences and relative, optional or other special rights, and qualifications, limitations or restrictions of such preferences or rights, of shares of such series not fixed and determined by law or in this Article III.

2. Distinctive Designations of Series . Each series of Preferred Stock shall be so designated as to distinguish the shares thereof from the shares of all other series. Different series of Preferred Stock shall not be considered to constitute different voting groups of shares for the purpose of voting by voting groups except as required by the VSCA or as otherwise specified by the Board of Directors with respect to any series at the time of the creation thereof.

3. Restrictions on Certain Distributions . So long as any shares of Preferred Stock are outstanding, the Corporation shall not declare and pay or set apart for payment any dividends (other than dividends payable in Common Stock or other stock of the Corporation ranking junior to the Preferred Stock as to dividends) or make any other distribution on such junior stock if, at the time of making such declaration, payment or distribution, the Corporation shall be in default with respect to any dividend payable on, or any obligation to redeem, any shares of Preferred Stock.

4. Redeemed or Reacquired Shares . Shares of any series of Preferred Stock that have been redeemed or otherwise reacquired by the Corporation (whether through the operation of a sinking fund, upon conversion or otherwise) shall have the status of authorized and unissued shares of Preferred Stock and may be redesignated and reissued as a part of such series (unless prohibited by the articles of amendment creating such series) or of any other series of Preferred Stock. Shares of Common Stock that have been reacquired by the Corporation shall have the status of authorized and unissued shares of Common Stock and may be reissued.

5. Voting Rights . Subject to the provisions of the VSCA or of the Bylaws of the Corporation as from time to time in effect with respect to the closing of the transfer books or the fixing of a record date for the determination of shareholders entitled to vote, and except as otherwise provided by the VSCA or in resolutions of the Board of Directors establishing any series of Preferred Stock pursuant to the provisions of paragraph 1 of this Article III, the holders of outstanding shares of Common Stock of the Corporation shall exclusively possess voting power for the election of directors and for all other purposes, with each holder of record of shares of Common Stock of the Corporation being entitled to one vote for each share of such stock standing in his name on the books of the Corporation.

6. No Preemptive Rights. No holder of shares of stock of any class of the Corporation shall, as such holder, have any right to subscribe for or purchase (a) any shares of stock of any class of the Corporation, or any warrants, options or other instruments that shall confer upon the holder thereof the right to subscribe for or purchase or receive from the Corporation any shares of stock of any class, whether or not such shares of stock, warrants, options or other instruments are issued for cash or services or property or by way of dividend or otherwise, or (b) any other security of the Corporation that shall be convertible into, or exchangeable for, any shares of stock of the Corporation of any class or classes, or to which shall be attached or appurtenant any warrant, option or other instrument that shall confer upon the holder of such security the right to subscribe for or purchase or receive from the Corporation any shares of its stock of any class or classes, whether or not such securities are issued for cash or services or property or by way of dividend or otherwise, other than such right, if any, as the Board of Directors, in its sole discretion, may from time to time determine. If the Board of Directors shall offer to the holders of shares of stock of any class of the Corporation, or any of them, any such shares of stock, options, warrants, instruments or other securities of the Corporation, such offer shall not, in any way, constitute a waiver or release of the right of the Board of Directors subsequently to dispose of other securities of the Corporation without offering the same to said holders.

7. Control Share Acquisition Statute. The provisions of Article 14.1 of the VSCA shall not apply to acquisitions of shares of any class of capital stock of the Corporation.

ARTICLE IV

1. The number of directors shall be as specified in the By-laws of the Corporation but such number may be increased or decreased from time to time in such manner as may be prescribed in the By-laws, provided that in no event shall the number of directors exceed twelve. In the absence of a By-law specifying the number of directors, the number shall be seven. Commencing with the 2000 annual meeting of shareholders (or by unanimous written consent in lieu thereof), the Board of Directors shall be divided into three classes, Class I, Class II, and Class III, as nearly equal in number as possible. The initial term of each class of directors shall expire at the annual meeting of shareholders to be held in the following years: Class I--2001; Class II--2002; and Class III--2003. At each annual meeting of shareholders after the 2000 annual meeting of shareholders, the successors to the class of directors whose term shall then expire shall be identified as being of the same class of directors they succeed and shall be elected to hold office for a term expiring at the third succeeding annual meeting of shareholders. When the number of directors is changed, any newly-created directorships or any decrease in directorships shall be so apportioned among the classes by the Board of Directors as to make all classes as nearly equal in number as possible; provided, however, that no decrease in the number of directors shall shorten or terminate the term of any incumbent director.

2. Subject to the rights of the holders of any Preferred Stock then outstanding, directors may be removed only with cause and only by the affirmative vote of at least 75 percent of the voting power of the then outstanding shares of capital stock of the Corporation entitled to vote generally in the election of directors ("Voting Stock"), voting together as a single voting group.

3. Subject to the rights of the holders of any Preferred Stock then outstanding and to any limitations set forth in the VSCA, newly-created directorships resulting from any increase in the number of directors and any vacancies in the Board of Directors resulting from death, resignation, disqualification, removal or other cause shall be filled solely (i) by the Board of Directors or (ii) at an annual meeting of shareholders by the shareholders entitled to vote on the election of directors. If the directors remaining in office constitute fewer than a quorum of the Board, they may fill the vacancy by the affirmative vote of a majority of the directors remaining in office.

4. Notwithstanding any other provision of the Articles of Incorporation or any provision of law that might otherwise permit a lesser vote, but in addition to any affirmative vote of the holders of any particular voting group required by the VSCA, the Articles of Incorporation or the terms of any Preferred Stock outstanding, the affirmative vote of at least 75 percent of the voting power of the then outstanding Voting Stock, voting together as a single voting group shall be required to alter, amend, repeal or adopt any provision inconsistent with any provision of this Article IV.

ARTICLE V

Except as expressly otherwise required in the Articles of Incorporation, an amendment or restatement of the Articles of Incorporation requiring shareholder approval shall be approved by a majority of the votes entitled to be cast by each voting group that is entitled to vote on the matter, unless in submitting any such amendment or restatement to the shareholders the Board of Directors shall require a greater vote.

ARTICLE VI

1. Every person who is or was a director, officer or employee of the Corporation, or who, at the request of the Corporation, serves or has served in any such capacity with another corporation, partnership, joint venture, trust, employee benefit plan, or other enterprise shall be indemnified by the Corporation against any and all liability and reasonable expense that may be incurred by him in connection with or resulting from any claim, action or proceeding (whether brought in the right of the Corporation or any such other corporation, entity, plan or otherwise), in which he may become involved, as a party or otherwise, by reason of his being or having been a director, officer or employee of the Corporation, or such other corporation, entity or plan while serving at the request of the Corporation, whether or not he continues to be such at the time such liability or expense is incurred, unless such person engaged in willful misconduct or a knowing violation of the criminal law.

As used in this Article VI: (a) the terms "liability" and "expense" shall include, but shall not be limited to, counsel fees and disbursements and amounts of judgments, fines or penalties against, and amounts paid in settlement by, a director, officer or employee; (b) the terms "director," "officer" and "employee," unless the context otherwise requires, include the estate or personal representative of any such person; (c) a person is considered to be serving an employee benefit plan as a director, officer or employee of the plan at the Corporation's request if his duties to the Corporation also impose duties on, or otherwise involve services by, him to the plan or, in connection with the plan, to participants in or beneficiaries of the plan; (d) the term "occurrence" means any act or failure to act, actual or alleged, giving rise to a claim, action or proceeding; and (e) service as a trustee or as a member of a management or similar committee of a partnership, joint venture or limited liability company shall be considered service as a director, officer or employee of the trust, partnership, joint venture or limited liability company.

The termination of any claim, action or proceeding, civil or criminal, by judgment, settlement, conviction or upon a plea of nolo contendere, or its equivalent, shall not create a presumption that a director, officer or employee did not meet the standards of conduct set forth in this paragraph 1. The burden of proof shall be on the Corporation to establish, by a preponderance of the evidence, that the relevant standards of conduct set forth in this paragraph 1 have not been met.

2. Any indemnification under paragraph 1 of this Article VI shall be made unless (a) the Board, acting by a majority vote of those directors who were directors at the time of the occurrence giving rise to the claim, action or proceeding involved and who are not at the time parties to such claim, action or proceeding (provided there are at least five such directors), finds that the director, officer or employee has not met the relevant standards of conduct set forth in such paragraph 1, or (b) if there are not at least five such directors, the Corporation's principal Virginia legal counsel, as last designated by the Board as such prior to the time of the occurrence giving rise to the claim, action or proceeding involved, or in the event for any reason such Virginia counsel is unwilling to so serve, then Virginia legal counsel mutually acceptable to the Corporation and the person seeking indemnification, deliver to the Corporation their written advice that, in their opinion, such standards have not been met.

3. Expenses incurred with respect to any claim, action or proceeding of the character described in paragraph 1 shall, except as otherwise set forth in this paragraph 3, be advanced by the Corporation prior to the final disposition thereof upon receipt of an undertaking by or on behalf of the recipient to repay such amount if it is ultimately determined that he is not entitled to indemnification under this Article VI. No security shall be required for such undertaking and such undertaking shall be accepted without reference to the recipient's final ability to make repayment. Notwithstanding the foregoing, the Corporation may refrain from, or suspend, payment of expenses in advance if at any time before delivery of the final finding described in paragraph 2, the Board or Virginia legal counsel, as the case may be, acting in accordance with the procedures set forth in paragraph 2, find by a preponderance of the evidence then available that the officer, director or employee has not met the relevant standards of conduct set forth in paragraph 1.

4. No amendment or repeal of this Article VI shall adversely affect or deny to any director, officer or employee the rights of indemnification provided in this Article VI with respect to any liability or expense arising out of a claim, action or proceeding based in whole or substantial part on an occurrence the inception of which takes place before or while this Article VI, as set forth in these Articles of Incorporation, is in effect. The provisions of this paragraph 4 shall apply to any such claim, action or proceeding whenever commenced, including any such claim, action or proceeding commenced after any amendment or repeal to this Article VI.

5. The rights of indemnification provided in this Article VI shall be in addition to any rights to which any such director, officer or employee may otherwise be entitled by contract or as a matter of law.

6. In any proceeding brought by or in the right of the Corporation or brought by or on behalf of shareholders of the Corporation, no director or officer of the Corporation shall be liable to the Corporation or its shareholders for monetary damages with respect to any transaction, occurrence or course of conduct, whether prior or subsequent to the effective date of this Article VI, except for liability resulting from such person's having engaged in willful misconduct or a knowing violation of the criminal law or any federal or state securities law.

ARTICLE VII

In furtherance of, and not in limitation of, the powers conferred by the VSCA, the Board of Directors is expressly authorized and empowered to adopt, amend or repeal the Bylaws of the Corporation; provided, however, that the Bylaws adopted by the Board of Directors under the powers hereby conferred may be altered, amended or repealed by the Board of Directors or by the shareholders having voting power with respect thereto, provided further that, in the case of any such action by shareholders, the affirmative vote of the holders of at least 75 percent of the voting power of the then outstanding Voting Stock, voting together as a single voting group, shall be required in order for the shareholders to alter, amend or repeal any provision of the Bylaws or to adopt any additional Bylaw. Notwithstanding any other provision of the Articles of Incorporation or any provision of law that might otherwise permit a lesser vote, but in addition to any affirmative vote of the holders of any particular voting group required by the VSCA, the Articles of Incorporation or the terms of any Preferred Stock outstanding, the affirmative vote of at least 75 percent of the voting power of the then outstanding Voting Stock, voting together as a single voting group, shall be required to alter, amend, repeal or adopt any provision inconsistent with any of the provisions of this Article VII.

ARTICLE VIII

The initial registered office shall be located at 951 E. Byrd Street, Riverfront Plaza, East Tower, in the City of Richmond, Virginia, and the initial registered agent shall be T. Justin Moore, III, who is a resident of Virginia and a member of the Virginia State Bar, and whose business address is the same as the address of the initial registered office.

/s/ T. Justin Moore, III
T. Justin Moore, III
Incorporator

ARTICLES OF AMENDMENT
of the
ARTICLES OF INCORPORATION
of
INSMED, INC.

These Articles of Amendment are filed in accordance with Section 13.1-710 of the Virginia Stock Corporation Act:

A. The name of the corporation (which is hereinafter referred to as the "Corporation") is Insmed, Inc.

B. The amendment to the Corporation's Articles of Incorporation adopted on March 13, 2000 by written consent of the Corporation's sole shareholder is as follows:

1. "ARTICLE I" of said Articles of Incorporation is deleted and is replaced by the following to change the name of the Corporation to Insmed Incorporated:

"ARTICLE I

The name of the Corporation shall be Insmed Incorporated."

C. The amendment was adopted by the written consent of the Corporation's sole shareholder.

INSMED, INC.

By: /s/ Michael D. Baer
Michael D. Baer
Chief Financial Officer

Dated: March 13, 2000

FORM OF
AMENDMENT TO ARTICLES OF INCORPORATION, AS AMENDED
TO CREATE A NEW SERIES OF PREFERRED STOCK
DESIGNATED AS
SERIES A JUNIOR PARTICIPATING PREFERRED STOCK
of
INSMED INCORPORATED

Pursuant to Section 13.1-639 of the Virginia Stock Corporation Act

I.

The name of the corporation is Insmed Incorporated (the "Company").

II.

Pursuant to Section 13.1-639 of the Virginia Stock Corporation Act and the authority conferred upon the Board of Directors by the Articles of Incorporation of the Company, as amended, the Articles of Incorporation are hereby amended to create a new series of shares of Preferred Stock, designated as "Series A Junior Participating Preferred Stock" by adding the following additional paragraph after the last paragraph of that Article III:

9. Series A Junior Participating Preferred Stock

(a) Designation and Amount . The shares of such series shall be designated as "Series A Junior Participating Preferred Stock" and the number of shares constituting such series shall be five hundred thousand (500,000).

(b) Dividends and Distributions .

1. Subject to the prior and superior rights of the holders of any shares of any series of Preferred Stock ranking prior and superior to the shares of Series A Junior Participating Preferred Stock with respect to dividends, the holders of shares of Series A Junior Participating Preferred Stock shall be entitled to receive, when, as and if declared by the Board of Directors out of funds legally available for the purpose, quarterly dividends payable in cash on the first day of January, April, July and October in each year (each such date being referred to herein as a "Quarterly Dividend Payment Date"), commencing on the first Quarterly Dividend Payment Date after the first issuance of a share or fraction of a share of Series A Junior Participating Preferred Stock, in an amount per share (rounded to the nearest cent) equal to the greater of (a) $1.00 or (b) subject to the provision for adjustment hereinafter set forth, 1000 times the aggregate per share amount of all cash dividends, and 1000 times the aggregate per share amount (payable in kind) of all non-cash dividends or other distributions other than a dividend payable in shares of Common Stock or a subdivision of the outstanding shares of Common Stock (by reclassification or otherwise), declared on the Common Stock, par value $.01 per share, of the Company (the "Common Stock") since the immediately preceding Quarterly Dividend Payment Date, or, with respect to the first Quarterly Dividend Payment Date, since the first issuance of any share or fraction of a share of Series A Junior Participating Preferred Stock. In the event the Company shall at any time after May 16, 2001 (the "Rights Declaration Date"), (i) declare any dividend on Common Stock payable in shares of Common Stock, (ii) subdivide the outstanding Common Stock or (iii) combine the outstanding Common Stock into a smaller number of shares, then in each such case the amount to which holders of shares of Series A Junior Participating Preferred Stock were entitled immediately prior to such event under clause (b) of the preceding sentence shall be adjusted by multiplying such amount by a fraction the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

2. The Company shall declare a dividend or distribution on the Series A Junior Participating Preferred Stock immediately after it declares a dividend or distribution on the Common Stock (other than a dividend payable in shares of Common Stock); provided that, in the event no dividend or distribution shall have been declared on the Common Stock during the period between any Quarterly Dividend Payment Date and the next subsequent Quarterly Dividend Payment Date, a dividend of $1.00 per share on the Series A Junior Participating Preferred Stock shall nevertheless be payable on such subsequent Quarterly Dividend Payment Date.

3. Dividends shall begin to accrue and be cumulative on outstanding shares of Series A Junior Participating Preferred Stock from the Quarterly Dividend Payment Date next preceding the date of issue of such shares of Series A Junior Participating Preferred Stock, unless the date of issue of such shares is prior to the record date for the first Quarterly Dividend Payment Date, in which case dividends on such shares shall begin to accrue from the date of issue of such shares, or unless the date of issue is a Quarterly Dividend Payment Date or is a date after the record date for the determination of holders of shares of Series A Junior Participating Preferred Stock entitled to receive a quarterly dividend and before such Quarterly Dividend Payment Date, in either of which events such dividends shall begin to accrue and be cumulative from such Quarterly Dividend Payment Date. Accrued but unpaid dividends shall not bear interest. Dividends paid on the shares of Series A Junior Participating Preferred Stock in an amount less than the total amount of such dividends at the time accrued and payable on such shares shall be allocated pro rata on a share-by-share basis among all such shares at the time outstanding. The Board of Directors may fix a record date for the determination of holders of shares of Series A Junior Participating Preferred Stock entitled to receive payment of a dividend or distribution declared thereon, which record date shall be no more than 30 days prior to the date fixed for the payment thereof.

(c) Voting Rights . The holders of shares of Series A Junior Participating Preferred Stock shall have the following voting rights:

1. Subject to the provision for adjustment hereinafter set forth, each share of Series A Junior Participating Preferred Stock shall entitle the holder thereof to 1000 votes on all matters submitted to a vote of the shareholders of the Company. In the event the Company shall at any time after the Rights Declaration Date (A) declare any dividend on Common Stock payable in shares of Common Stock, (B) subdivide the outstanding Common Stock or (C) combine the outstanding Common Stock into a smaller number of shares, then in each such case the number of votes per share to which holders of shares of Series A Junior Participating Preferred Stock were entitled immediately prior to such event shall be adjusted by multiplying such number by a fraction the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

2. Except as otherwise provided herein or by law, the holders of shares of Series A Junior Participating Preferred Stock and the holders of shares of Common Stock shall vote together as one class on all matters submitted to a vote of shareholders of the Company.

(A) If at any time dividends on any Series A Junior Participating Preferred Stock shall be in arrears in an amount equal to six quarterly dividends thereon, the occurrence of such contingency shall mark the beginning of a period (herein called a "Default Period") that shall extend until such time when all accrued and unpaid dividends for all previous quarterly dividend periods and for the current quarterly dividend period on all shares of Series A Junior Participating Preferred Stock then outstanding shall have been declared and paid or set apart for payment. During each Default Period, all holders of Preferred Stock (including holders of the Series A Junior Participating Preferred Stock) with dividends in arrears in an amount equal to six quarterly dividends thereon, voting as a class, irrespective of series, shall have the right to elect two directors.

(B) During any Default Period, such voting right of the holders of Series A Junior Participating Preferred Stock may be exercised initially at a special meeting called pursuant to Paragraph (c)2.(C) or at any annual meeting of shareholders, and thereafter at annual meetings of shareholders, provided that neither such voting right nor the right of the holders of any other series of Preferred Stock, if any, to increase, in certain cases, the authorized number of directors shall be exercised unless the holders of ten percent in number of shares of Preferred Stock outstanding shall be present in person or by proxy. The absence of a quorum of the holders of Common Stock shall not affect the exercise by the holders of Preferred Stock of such voting right. At any meeting at which the holders of Preferred Stock shall exercise such voting right initially during an existing Default Period, they shall have the right, voting as a class, to elect directors to fill such vacancies, if any, in the Board of Directors as may then exist up to two directors or, if such right is exercised at an annual meeting, to elect two directors. If the number that may be so elected at any special meeting does not amount to the required number, the holders of the Preferred Stock shall have the right to make such increase in the number of directors as shall be necessary to permit the election by them of the required number. After the holders of the Preferred Stock shall have exercised their right to elect directors in any Default Period and during the continuance of such period, the number of directors shall not be increased or decreased except by vote of the holders of Preferred Stock as herein provided or pursuant to the rights of any equity securities ranking senior to or pari passu with the Series A Junior Participating Preferred Stock.

(C) Unless the holders of Preferred Stock shall, during an existing Default Period, have previously exercised their right to elect directors, the Board of Directors may order, or any shareholder or shareholders owning in the aggregate not less than ten percent of the total number of shares of Preferred Stock outstanding, irrespective of series, may request, the calling of a special meeting of the holders of Preferred Stock, which meeting shall thereupon be called by the President, a Vice President or the Secretary of the Company. Notice of such meeting and of any annual meeting at which holders of Preferred Stock are entitled to vote pursuant to this Paragraph (c)2.(C) shall be given to each holder of record of Preferred Stock by mailing a copy of such notice to him at his last address as the same appears on the books of the Company. Such meeting shall be called for a time not earlier than 20 days and not later than 60 days after such order or request or in default of the calling of such meeting within 60 days after such order or request, such meeting may be called on similar notice by any shareholder or shareholders owning in the aggregate not less than ten percent of the total number of shares of Preferred Stock outstanding. Notwithstanding the provisions of this Paragraph (c)2.(C), no such special meeting shall be called during the period within 60 days immediately preceding the date fixed for the next annual meeting of the shareholders.

(D) In any Default Period, the holders of Common Stock, and other classes of stock of the Company if applicable, shall continue to be entitled to elect the whole number of directors until the holders of Preferred Stock shall have exercised their right to elect two directors voting as a class, after the exercise of which right (x) the directors so elected by the holders of Preferred Stock shall continue in office until their successors shall have been elected by such holders or until the expiration of the Default Period, and (y) any vacancy in the Board of Directors may (except as provided in Paragraph (c)2.(C) above) be filled by vote of a majority of the remaining directors theretofore elected by the holders of the class of stock that elected the director whose office shall have become vacant. References in this Paragraph (c) to directors elected by the holders of a particular class of stock shall include directors elected by such directors to fill vacancies as provided in clause (y) of the foregoing sentence.

(E) Immediately upon the expiration of a Default Period, (I) the right of the holders of Preferred Stock as a class to elect directors shall cease, (II) the term of any directors elected by the holders of Preferred Stock as a class shall terminate and (III) the number of directors shall be such number as may be provided for in the Articles of Incorporation, as amended or Amended and Restated Bylaws irrespective of any increase made pursuant to the provisions of Paragraph (c)2.(A) (such number being subject, however, to change thereafter in any manner provided by law or in the Articles of Incorporation, as amended or Amended and Restated Bylaws). Any vacancies in the Board of Directors effected by the provisions of clauses (II) and (III) in the preceding sentence may be filled by a majority of the remaining directors.

2. Except as set forth herein, holders of Series A Junior Participating Preferred Stock shall have no special voting rights, and their consent shall not be required (except to the extent they are entitled to vote with holders of Common Stock as set forth herein) for taking any corporate action.

(d) Certain Restrictions .

1. Whenever quarterly dividends or other dividends or distributions payable on the Series A Junior Participating Preferred Stock as provided in Paragraph (b) above are in arrears, thereafter and until all accrued and unpaid dividends and distributions, whether or not declared, on shares of Series A Junior Participating Preferred Stock outstanding shall have been paid in full, the Company shall not:

(A) declare or pay dividends on, make any other distributions on, or redeem or purchase or otherwise acquire for consideration any shares of stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Series A Junior Participating Preferred Stock;

(B) declare or pay dividends on or make any other distributions on any shares of stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with the Series A Junior Participating Preferred Stock, except dividends paid ratably on the Series A Junior Participating Preferred Stock and all such parity stock on which dividends are payable or in arrears in proportion to the total amounts to which the holders of all such shares are then entitled;

(C) redeem or purchase or otherwise acquire for consideration shares of any stock ranking on a parity (either as to dividends or upon liquidation, dissolution or winding up) with the Series A Junior Participating Preferred Stock, provided that the Company may at any time redeem, purchase or otherwise acquire shares of any such parity stock in exchange for shares of any stock of the Company ranking junior (either as to dividends or upon dissolution, liquidation or winding up) to the Series A Junior Participating Preferred Stock; or

(D) purchase or otherwise acquire for consideration any shares of Series A Junior Participating Preferred Stock, or any shares of stock ranking on a parity with the Series A Participating Preferred Stock, except in accordance with a purchase offer made in writing or by publication (as determined by the Board of Directors) to all holders of such shares upon such terms as the Board of Directors, after consideration of the respective annual dividend rates and other relative rights and preferences of the respective series and classes, shall determine in good faith will result in fair and equitable treatment among the respective series or classes.

2. The Company shall not permit any subsidiary of the Company to purchase or otherwise acquire for consideration any shares of stock of the Company unless the Company could, under Paragraph (d)1. , purchase or otherwise acquire such shares at such time and in such manner.

(e) Reacquired Shares . Any shares of Series A Junior Participating Preferred Stock purchased or otherwise acquired by the Company in any manner whatsoever shall be retired and cancelled promptly after the acquisition thereof. All such shares shall upon their cancellation become authorized but unissued shares of Preferred Stock to be created by resolution or resolutions of the Board of Directors, subject to the conditions and restrictions on issuance set forth herein.

(f) Liquidation, Dissolution or Winding Up .

1. Upon any liquidation (voluntary or otherwise), dissolution or winding up of the Company, no distribution shall be made to the holders of shares of stock ranking junior (either as to dividends or upon liquidation, dissolution or winding up) to the Series A Junior Participating Preferred Stock unless, prior thereto, the holders of shares of Series A Junior Participating Preferred Stock shall have received $100 per share, plus an amount equal to accrued and unpaid dividends and distributions thereon, whether or not declared, to the date of such payment (the "Series A Liquidation Preference"). Following the payment of the full amount of the Series A Liquidation Preference, no additional distributions shall be made to the holders of shares of Series A Junior Participating Preferred Stock unless, prior thereto, the holders of shares of Common Stock shall have received an amount per share (the "Common Adjustment") equal to the quotient obtained by dividing (A) the Series A Liquidation Preference by (B) 1000 (as appropriately adjusted as set forth in subparagraph 3 . below to reflect such events as stock splits, stock dividends and recapitalizations with respect to the Common Stock) (such number in clause (ii), the "Adjustment Number"). Following the payment of the full amount of the Series A Liquidation Preference and the Common Adjustment in respect of all outstanding shares of Series A Junior Participating Preferred Stock and Common Stock, respectively, holders of Series A Junior Participating Preferred Stock and holders of shares of Common Stock shall receive their ratable and proportionate share of the remaining assets to be distributed in the ratio of the Adjustment Number to one with respect to such Preferred Stock and Common Stock, on a per share basis, respectively.

2. In the event, however, that there are not sufficient assets available to permit payment in full of the Series A Liquidation Preference and the liquidation preferences of all other series of Preferred Stock, if any, that rank on a parity with the Series A Junior Participating Preferred Stock, then such remaining assets shall be distributed ratably to the holders of such parity shares in proportion to their respective liquidation preferences. In the event, however, that there are not sufficient assets available to permit payment in full of the Common Adjustment, then such remaining assets shall be distributed ratably to the holders of Common Stock.

3. In the event the Company shall at any time after the Rights Declaration Date (A) declare any dividend on Common Stock payable in shares of Common Stock, (B) subdivide the outstanding Common Stock or (C) combine the outstanding Common Stock into a smaller number of shares, then in each such case the Adjustment Number in effect immediately prior to such event shall be adjusted by multiplying such Adjustment Number by a fraction, the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

(g) Consolidation, Merger, etc. In case the Company shall enter into any consolidation, merger, combination or other transaction in which the shares of Common Stock are exchanged for or changed into other stock or securities, cash and/or any other property, then in any such case the shares of Series A Junior Participating Preferred Stock shall at the same time be similarly exchanged or changed in an amount per share (subject to the provision for adjustment hereinafter set forth) equal to 1000 times the aggregate amount of stock, securities, cash and/or any other property (payable in kind), as the case may be, into which or for which each share of Common Stock is changed or exchanged. In the event the Company shall at any time after the Rights Declaration Date (i) declare any dividend on Common Stock payable in shares of Common Stock, (ii) subdivide the outstanding Common Stock, or (iii) combine the Outstanding Common Stock into a smaller number of shares, then in each such case the amount set forth in the preceding sentence with respect to the exchange or change of shares of Series A Junior Participating Preferred Stock shall be adjusted by multiplying such amount by a fraction the numerator of which is the number of shares of Common Stock outstanding immediately after such event and the denominator of which is the number of shares of Common Stock that were outstanding immediately prior to such event.

(h) No Redemption . The shares of Series A Junior Participating Preferred Stock shall not be redeemable.

(i) Ranking . The Series A Junior Participating Preferred Stock shall rank junior to all other series of the Company's Preferred Stock as to the payment of dividends and the distribution of assets, unless the terms of any such series shall provide otherwise.

(j) Amendment . At any time when any shares of Series A Junior Participating Preferred Stock are outstanding, the Articles of Incorporation of the Company, as amended, and as amended hereby, shall not be amended in any manner that would materially alter or change the powers, preferences or special rights of the Series A Junior Participating Preferred Stock so as to affect them adversely without the affirmative vote of the holders of a majority or more of the then outstanding shares of Series A Junior Participating Preferred Stock, voting separately as a class.

(k) Fractional Shares . Series A Junior Participating Preferred Stock may be issued in fractions of a share which shall entitle the holder, in proportion to such holder's fractional shares, to exercise voting rights, receive dividends, participate in distributions and to have the benefit of all other rights of holders of Series A Junior Participating Preferred Stock.

IV.

The foregoing amendment was duly adopted by the Company's Board of Directors on May 16, 2001. No shareholder action was required.

INSMED INCORPORATED

Dated: May 16, 2001

By: /s/ Geoffrey Allan
Geoffrey Allan, Ph.D.
Chairman of the Board, President and Chief Executive Officer

Articles of Amendment
to the
Articles of Incorporation, as amended,
of
INSMED INCORPORATED

I.

The name of the corporation is Insmed Incorporated (the "Company").

II.

Article III of the Company's Articles of Incorporation, as amended, shall be amended by the addition of the following additional paragraph after the last paragraph of that Article III:

8. Reverse Stock Split. Simultaneously with the effective date of this amendment (the "Effective Time"), each four shares of the Company's Common Stock, par value $.01 per share, issued and outstanding immediately prior to the Effective Time (the "Old Common Stock") shall, automatically and without any action on the part of the holder thereof, be reclassified as and changed, pursuant to a reverse stock split (the "Reverse Split"), into one share of the Company's outstanding Common Stock (the "New Common Stock"), subject to the treatment of fractional share interests as described below. Each holder of a certificate or certificates which immediately prior to the Effective Time represented outstanding shares of Old Common Stock (the "Old Certificates," whether one or more) shall be entitled to receive upon surrender of such Old Certificates to the Company's Transfer Agent for cancellation, a certificate or certificates (the "New Certificates," whether one or more) representing the number of whole shares of the New Common Stock into and for which the shares of the Old Common Stock formerly represented by such Old Certificates so surrendered, are reclassified under the terms hereof. From and after the Effective Time, Old Certificates shall thereupon be deemed for all corporate purposes to evidence ownership of New Common Stock in the appropriately reduced whole number of shares. No certificates or scrip representing fractional share interests in New Common Stock will be issued, and no such fractional share interest will entitle the holder thereof to vote, or to any rights of a shareholder of the Company. In lieu of any fraction of a share of New Common Stock to which the holder would otherwise be entitled, the holder will receive a cash payment in U.S. dollars equal to such fraction multiplied by four times the average of the closing bid and ask price per share of Common Stock as quoted on The Nasdaq SmallCap Market for the five trading days immediately preceding the Effective Time. If more than one Old Certificate shall be surrendered at one time for the account of the same shareholder, the number of full shares of New Common Stock for which New Certificates shall be issued shall be computed on the basis of the aggregate number of shares represented by the Old Certificates so surrendered. In the event that the Company's Transfer Agent determines that a holder of Old Certificates has not surrendered all his certificates for exchange, the Transfer Agent shall carry forward any fractional share until all certificates of that holder have been presented for exchange such that payment for fractional shares to any one person shall not exceed the value of one share.

If any New Certificate is to be issued in a name other than that in which it was issued, the Old Certificates so surrendered shall be properly endorsed and otherwise in proper form for transfer, and the stock transfer tax stamps to the Old Certificates so surrendered shall be properly endorsed and otherwise in proper form for transfer, and the person or persons requesting such exchange shall affix any requisite stock transfer tax stamps to the Old Certificates surrendered, or provide funds for their purchase, or establish to the satisfaction of the Transfer Agent that such taxes are not payable. From and after the Effective Time, the amount of capital shall be represented by the shares of the New Common Stock into which and for which the shares of the Old Common Stock are reclassified, until thereafter reduced or increased in accordance with applicable law. All references elsewhere in the Articles of Incorporation, as amended, to the "Common Stock" shall, after the Effective Time, refer to the "New Common Stock".

III.

The amendment was proposed by the board of directors and submitted to the shareholders of the Company in accordance with Chapter 9 of Title 13.1 of the Code of Virginia. The designation, number of outstanding shares, and number of votes entitled to be cast by each voting group entitled to vote separately on the amendment are as follows:

Designation	Number of Outstanding Shares	Number of Votes
Common	108,127,568	108,127,568

The total number of undisputed votes cast for the amendment by each voting group was as follows:

Designation	Number of Undisputed Votes for the Amendment
Common	93,583,881

The number of votes cast for the amendment by each voting group was sufficient for approval by that voting group.

IV.

Pursuant to Section 13.1-606 of the Virginia Stock Corporation Act, the effective time and date of this Amendment to the Company's Articles of Incorporation, as amended, shall be 11:59 p.m. on July 28, 2000.

INSMED INCORPORATED

Dated: July 28, 2000

By: /s/ Geoffrey Allan
Geoffrey Allan, Ph.D.
Chairman of the Board, President and Chief Executive Officer

ARTICLES OF AMENDMENT
TO THE
ARTICLES OF INCORPORATION, AS AMENDED,
of
INSMED INCORPORATED
TO CREATE A NEW SERIES OF PREFERRED STOCK
DESIGNATED AS
SERIES B CONDITIONAL CONVERTIBLE PREFERRED STOCK

Pursuant to Section 13.1-639 of the Virginia Stock Corporation Act

I.

The name of the corporation is Insmed Incorporated (the " Company ").

II.

Pursuant to Section 13.1-639 of the Virginia Stock Corporation Act and the authority conferred upon the Board of Directors by the Articles of Incorporation, as amended, the Articles of Incorporation are hereby amended to create a new series of shares of Preferred Stock, designated as "Series B Conditional Convertible Preferred Stock" by adding the following additional paragraph after the last paragraph of Article III:

10. *Series B Conditional Convertible Preferred Stock*

(a) Designation . The designation of the series of preferred stock of the Company is "Series B Conditional Convertible Preferred Stock", par value $0.01 per share (the " Series B Preferred Stock "). Each share of Series B Preferred Stock shall be identical in all respects to every other share of Series B Preferred Stock.

(b) Number of Shares . The authorized number of shares of Series B Preferred Stock is 92,000,000. Shares of Series B Preferred Stock that are purchased or otherwise acquired by the Company, shall revert to authorized but unissued shares of Preferred Stock.

(c) Defined Terms . As used herein with respect to the Series B Preferred Stock:

" Affiliate " shall mean, with respect to any specified Person, any other Person that directly or indirectly controls, is controlled by or is under common control with such specified Person. For the purposes of this definition, the term "control," when used with respect to any specified Person, means the power to direct or cause the direction of the management or policies of such Person, directly or indirectly, whether through the ownership of voting securities, by contract or otherwise; and the terms "controlling" and "controlled" have correlative meanings.

" Articles of Amendment " shall mean these Articles of Amendment relating to the Series B Preferred Stock, as it may be amended from time to time.

" Articles of Incorporation " shall mean the Articles of Incorporation of the Company, as amended from time to time, including by these Articles of Amendment.

" Beneficially Own " shall mean "beneficially own" as defined in Rule 13d-3 under the Exchange Act.

" Board of Directors " shall mean the board of directors of the Company.

" Business Day " shall mean any day that is not a Saturday, Sunday or legal holiday in New York City or a federal holiday in the United States.

" Bylaws " shall mean the Amended and Restated Bylaws of the Company in effect on the Original Issue Date, as they may be amended from time to time.

" Capital Stock " shall mean: (1) any shares, interests, participations or other equivalents (however designated) of capital stock of a corporation; (2) any ownership interests in a Person other than a corporation, including membership interests, partnership interests, joint venture interests and beneficial interests; and (3) any warrants, options, convertible or exchangeable securities, subscriptions, rights (including any preemptive or similar rights), calls or other rights to purchase or acquire any of the foregoing.

" Change of Control " shall mean the occurrence of any of the following: (1) the direct or indirect sale, transfer, conveyance, lease or other disposition (other than by way of merger or consolidation), in one or a series of related transactions, of all or substantially all of the properties or assets of the Company and its Subsidiaries, taken as a whole, to any "person" (as that term is used in Section 13(d)(3) of the Exchange Act) other than a pledge or grant of a security interest to a bona fide lender; (2) any "person" or "group" (as such terms are used in Sections 13(d) and 14(d) of the Exchange Act), shall Beneficially Own, directly or indirectly, through a purchase, merger or other acquisition transaction or series of transactions, shares of the Company's Capital Stock entitling such Person to exercise a majority of the total voting power of all classes of Voting Stock of the Company; (3) the Company merges or consolidates with or into any other "person" (as that term is used in Section 13(d)(3) of the Exchange Act) or another "person" (as that term is used in Section 13(d)(3) of the Exchange Act) merges with or into the Company and, as a result of such transaction, the shareholders of the Company immediately prior to such transaction shall Beneficially Own less than a majority of the total voting power of all classes of Voting Stock of the Company; or (4) the Company engages in any recapitalization, reclassification or other transaction in which a majority of the Common Stock is exchanged for or converted into cash, securities or other property, in each case, other than a merger, consolidation, recapitalization, reclassification or other transaction (A) that does not result in a reclassification, conversion, exchange or cancellation of the Company's outstanding Common Stock; (B) which is effected solely to change the Company's jurisdiction of incorporation and results in a reclassification, conversion or exchange of outstanding shares of Common Stock solely into shares of common stock of the surviving entity; or (C) where the Voting Stock of the Company outstanding immediately prior to such transaction is converted or exchanged for Voting Stock of the surviving or transferee Person constituting a majority of the outstanding shares of such Voting Stock of such surviving or transferee Person (immediately after giving effect to such issuance).

For purposes of this definition, (i) any direct or indirect holding company of the Company shall not itself be considered a "person" or "group" for purposes of clauses (2) and (3) above, provided that no "person" or "group" (other than another such holding company) Beneficially Owns, directly or indirectly, a majority of the voting power of the Voting Stock of such holding company, and a majority of the Voting Stock of such holding company immediately following it becoming the holding company of the Company is Beneficially Owned by the Persons who Beneficially Owned the voting power of the Voting Stock of the Company immediately prior to it becoming such holding company and (ii) a Person shall not be deemed to have beneficial ownership of securities subject to a stock purchase agreement, merger agreement or similar agreement until the consummation of the transactions contemplated by such agreement.

" Close of Business " shall mean 5:00 p.m., eastern time, on any Business Day.

" Closing Price " shall mean, with respect to a share of Capital Stock of a Person, on the applicable Trading Day (a) if the Capital Stock is listed on a national securities exchange, the closing price per share of Capital Stock on such date published in The Wall Street Journal (National Edition) or, if no such closing price on such date is published in The Wall Street Journal (National Edition) , the average of the closing bid and asked prices on such date, as officially reported on the principal national securities exchange on which the Capital Stock is then listed or admitted to trading; or (b) if the Capital Stock is not listed or admitted to trading on any national securities exchange, the last sale price or, if such last sale price is not reported, the average of the high bid and low asked prices on the automatic quotation system on which the Capital Stock is then listed, as reported by Bloomberg Financial Markets (or any successor thereto); or (c) if on any such date the Capital Stock is not quoted on any such automatic quotation system, the average of the closing bid and asked prices as furnished by a professional market maker making a market in the Capital Stock selected by the Company; or (d) if none of (a), (b) or (c) is applicable, a market price per share determined in good faith by the Board of Directors and the holders of at least 62.5% of the then outstanding Series B Preferred Stock.

" Code " shall mean the Internal Revenue Code of 1986, as amended.

" Commission " shall mean the U.S. Securities and Exchange Commission, including the staff thereof.

" Common Stock " shall mean the common stock, par value $0.01 per share, of the Company.

" Company " shall mean Insmed Incorporated, a corporation organized and existing under the laws of the Commonwealth of Virginia, and any successor thereof.

" Conversion Price " shall mean $0.7114, subject to adjustment as set forth in Paragraph (g) of this Section 10.

" Exchange Act " shall mean the Securities Exchange Act of 1934, as amended.

" Governmental Authority " means: (1) any federal, state, local, foreign or international government or governmental authority, regulatory or administrative agency, governmental commission, department, board, bureau, agency or instrumentality, court, tribunal, arbitrator or arbitral body (public or private); (2) any self-regulatory organization; or (3) any political subdivision of any of the foregoing.

" Junior Stock " shall mean the Common Stock, the Series A Preferred Stock and any other class or series of Capital Stock that ranks junior to the Series B Preferred Stock (i) as to the payment of dividends or (ii) as to the distribution of assets on any liquidation, dissolution or winding up of the Company, or both.

" Mandatory Conversion Date " shall mean the date the Shareholder Approval is obtained.

" Milestone Date " shall mean the earlier of (i) December 1, 2011 and (ii) the first date upon which at least 50 patients have been given at least one dose in Phase III clinical trials for Arikace™, but in no event earlier than September 1, 2011.

" Original Issue Date " shall mean December 1, 2010.

" Original Holders " shall mean the holders of the Series B Preferred Stock as of the Original Issue Date and their respective Affiliates and any limited partners, members or other similar equity holders of any holder of Series B Preferred Stock as of the Original Issue Date that receive shares of Series B Preferred Stock as a distribution pursuant to such holder's limited partnership agreement, limited liability company agreement, operating agreement or similar governing document.

" Parity Stock " shall mean any class or series of Capital Stock that ranks equally with the Series B Preferred Stock both (i) in the priority of payment of dividends and (ii) in the distribution of assets upon any liquidation, dissolution or winding up of the Company (in each case, without regard to whether dividends accrue cumulatively or non-cumulatively).

" Person " means any natural person, business, corporation, company, partnership, association, limited liability company, limited partnership, limited liability partnership, joint venture, business enterprise, trust or other legal entity, including any Governmental Authority.

" Preferred Stock " shall mean any and all series of preferred stock of the Company, including the Series B Preferred Stock.

" Record Date " shall mean the date fixed for determination of shareholders of the Company entitled to notice of or to vote at any meeting of shareholders of the Company or any adjournment thereof, or entitled to receive payment of any dividend, or in order to make a determination of the shareholders of the Company for any other proper purpose (whether such date is fixed by the Board of Directors or by statute, contract, these Articles of Amendment or otherwise).

" Series A Preferred Stock " shall mean the Series A Junior Participating Preferred Stock of the Company.

" Series B Preferred Stock " shall have the meaning ascribed to it in Paragraph (a) of this Section 10.

" Shareholder Approval " shall mean all approvals of the shareholders of the Company necessary to approve, for purposes of the NASDAQ Listing Rules, the conversion of the Series B Preferred Stock into shares of Common Stock.

" Stated Value " shall mean $0.7114 per share of Series B Preferred Stock, which may increased as provided in Paragraph (d)(2) of this Section 10. The Stated Value shall be equitably adjusted from time to time by the Board of Directors to reflect fully the appropriate effect of any stock split, reverse stock split, stock dividend (including any dividend or distribution of securities convertible into Series B Preferred Stock), reorganization, recapitalization, reclassification or similar change with respect to shares of Series B Preferred Stock having a Record Date on or after the Original Issue Date.

" Subsidiary " shall mean any company, partnership, limited liability company, joint venture, joint stock company, trust, unincorporated organization or other entity for which the Company owns at least 50% of the Voting Stock of such entity.

" Trading Day " shall mean any Business Day on which the Common Stock is traded, or able to be traded, on the principal national securities exchange on which the Common Stock is listed or admitted to trading; provided that if the Common Stock is not listed or admitted to trading on a national securities exchange, Trading Day shall mean any Business Day on which the NASDAQ Capital Market is generally open.

" Voting Stock " shall mean Capital Stock of the class or classes pursuant to which the holders thereof have the general voting power under ordinary circumstances (determined without regard to any classification of directors) to elect one or more members of the Board of Directors (without regard to whether or not, at the relevant time, Capital Stock of any other class or classes (other than Common Stock) shall have or might have voting power by reason of the happening of any contingency).

(d) Dividends .

1. In the event that the Company shall declare a dividend or make any other distribution (including in cash, in Capital Stock (including any options, warrants or other rights to acquire Capital Stock) of the Company, whether or not pursuant to a shareholder rights plan, "poison pill" or similar arrangement, or other property or assets) to holders of Common Stock, then the Board of Directors shall declare, and the holder of each share of Series B Preferred Stock shall be entitled to receive, a dividend or distribution, as applicable, in an amount equal to the amount of such dividend or distribution, as applicable, received by a holder of the number of shares of Common Stock for which such share of Series B Preferred Stock is convertible on the Record Date for such dividend or distribution (whether or not such holder of shares of Series B Preferred Stock had been eligible to convert its shares of Series B Preferred Stock on such date). Any such amount shall be paid to the holders of shares of Series B Preferred Stock at the same time such dividend or distribution, as applicable, is paid to holders of Common Stock.

2. Commencing on the Milestone Date, in addition to participation in dividends on Common Stock as set forth in Paragraph (d)(1) of this Section 10, holders of shares of Series B Preferred Stock shall be entitled to receive, on each share of Series B Preferred Stock, dividends at an annual rate of 12.5% of the Stated Value payable at the end of each six month period following the Milestone Date. Dividends payable pursuant to this Paragraph (d)(2) with respect to any share of Series B Preferred Stock shall accrue daily from and after the Milestone Date, whether or not the Company has funds legally available for such dividends or such dividends are declared and shall be calculated on the basis of a 360-day year. Dividends that are payable on shares of Series B Preferred Stock pursuant to this Paragraph (d)(2) shall be payable in cash except that, at the option of the Board of Directors, such dividends may be paid in kind by increasing the Stated Value by the amount of such dividend. Dividends that are payable on shares of Series B Preferred Stock shall be payable to holders of record of the shares of Series B Preferred Stock as they appear on the stock register of the Company on the Record Date for such dividend, which shall be no more than sixty (60) days or less than ten (10) days prior to the date fixed for payment thereof.

3. The holders of shares of Series B Preferred Stock shall not be entitled to receive any dividends or other distributions except as provided herein.

(e) Liquidation Rights .

1. Voluntary or Involuntary Liquidation . In the event of (i) any liquidation, dissolution or winding up of the affairs of the Company, whether voluntary or involuntary, or (ii) any Change of Control (clauses (i) and (ii) are herein referred to as a " Deemed Liquidation Event "), holders of the Series B Preferred Stock shall be entitled to receive for each share of Series B Preferred Stock, out of the assets of the Company or proceeds thereof (whether capital or surplus) available for distribution to shareholders of the Company, and after satisfaction of all liabilities and obligations to creditors of the Company, on par with each share of Parity Stock but before any distribution of such assets or proceeds is made to or set aside for the holders of Junior Stock, an amount equal to the greater of (x) the sum of (A) the Stated Value per share of Series B Preferred Stock *plus* (B) an amount per share of Series B Preferred Stock equal to the accrued but unpaid dividends to which such holder of shares of Series B Preferred Stock is entitled to receive pursuant to Paragraph (d)(2) of this Section 10 to but excluding the date fixed for such Deemed Liquidation Event, if any, and (y) the per share amount of all cash, securities and other property (such securities or other property having a value equal to its fair market value as reasonably determined by the Board of Directors) to be distributed in respect of the Common Stock that such holder of Series B Preferred Stock would have been entitled to receive had it converted such Series B Preferred Stock immediately prior to the date fixed for such Deemed Liquidation Event (whether or not such holder of shares of Series B Preferred Stock had been eligible to convert its shares of Series B Preferred Stock on such date) (such greater amount being the " Series B Liquidation Amount "). To the extent such amount is paid in full to all holders of Series B Preferred Stock and all the holders of Parity Stock, the holders of Junior Stock of the Company shall be entitled to receive all remaining assets of the Company (or proceeds thereof) according to their respective rights and preferences.

2. Partial Payment . If, in connection with any distribution described in Paragraph (e)(1) of this Section 10, the assets of the Company or proceeds thereof are not sufficient to pay the Series B Liquidation Amount in full to all holders of Series B Preferred Stock and all holders of Parity Stock, if any, the amounts paid to the holders of Series B Preferred Stock and to the holders of all such other Parity Stock shall be paid *pro rata* in accordance with the respective aggregate amounts payable to the holders of Series B Preferred Stock and the amounts payable to holders of all such other Parity Stock pursuant to Paragraph (e)(1) of this Section 10.

(f) Conversion .

1. Mandatory Conversion . Each share of Series B Preferred Stock shall be automatically converted, immediately at the Close of Business on the Mandatory Conversion Date, with no further action required to be taken by the Company or the holder thereof, into the number of shares of Common Stock equal to the number obtained by dividing (x) the sum of (A) the Stated Value *plus* (B) except to the extent paid in cash as contemplated by Paragraph (f)(2) of this Section 10 at the time of the conversion, an amount per share of Series B Preferred Stock equal to the accrued but unpaid dividends to which such holder of shares of Series B Preferred Stock is entitled to receive pursuant to Paragraph (d)(2) of this Section 10 through, but excluding, the conversion date, if any, by (y) the Conversion Price in effect at such time. Immediately upon conversion as provided herein (i) each holder of Series B Preferred Stock shall be deemed to be the holder of record of the Common Stock issuable upon conversion of such holder's shares of Series B Preferred Stock, notwithstanding that the share register of the Company shall then be closed or that book-entry evidence shall not then actually be delivered to such Person and (ii) each converted shares of Series B Preferred Stock as provided herein shall be retired and cancelled automatically with no further action required to be taken by the Company or the holder thereof. As promptly as practicable on or after the Mandatory Conversion Date (and in any event no later than five Trading Days thereafter), the Company shall provide notice to the holders of the Series B Preferred Stock of the occurrence of the Mandatory Conversion Date, which notice shall set forth procedures for the surrender of the shares of Series B Preferred Stock which have been converted to the office of the Company. The Company shall promptly issue the number of whole shares of Common Stock issuable upon conversion against the surrender of the shares of Series B Preferred Stock. Any shares of Common Stock issuable upon conversion of shares of Series B Preferred Stock shall be delivered by the Company to the appropriate holder on a book-entry basis. To the extent that Company has a shareholders rights plan, "poison pill" or similar arrangement in effect with respect to the Common Stock on the Mandatory Conversion Date, upon conversion of any shares of the Series B Preferred Stock, the holders thereof will receive, in addition to the shares of Common Stock, the rights under such shareholders rights plan, "poison pill" or similar arrangement.

2. Option to Pay Accrued Dividends in Cash . When shares of Series B Preferred Stock are converted pursuant to this Paragraph (f), all dividends accrued but not yet paid on the Series B Preferred Stock so converted from and including the Milestone Date to and including the date of conversion may, at the election of the Company, be paid, in whole or in part, in cash; it being understood that the amount of any accrued dividend so paid in cash shall reduce the amount added to the Stated Value pursuant to clause (B) of Paragraph (f)(1) of this Section 10.

3. Common Stock Reserved for Issuance . The Company shall at all times reserve and keep available out of its authorized and unissued Common Stock and Series A Preferred Stock, solely for issuance upon the conversion of the Series B Preferred Stock, such number of shares of Common Stock (and associated rights evidenced by the Series A Preferred Stock) as shall from time to time be issuable upon the conversion of all the shares of Series B Preferred Stock then outstanding. Any shares of Common Stock (and associated rights evidenced by the Series A Preferred Stock) issued upon conversion of Series B Preferred Stock shall be (i) duly authorized, validly issued and fully paid and nonassessable, (ii) shall rank *pari passu* with the other shares of Common Stock outstanding from time to time and (iii) shall be free from any preemptive rights or similar rights and any liens, charges, security interest or other encumbrances (unless created by the holder thereof). The Company hereby covenants and agrees that, if at any time the Common Stock shall be listed on The NASDAQ Capital Market or any other national securities exchange or automated quotation system, the Company will, if permitted by the rules of such exchange or automated quotation system, list and keep listed, so long as the Common Stock shall be so listed on such exchange or automated quotation system, all the Common Stock issuable upon conversion of the Series B Preferred Stock; *provided, however* , that if the rules of such exchange or automated quotation system permit the Company to defer the listing of such Common Stock until the first conversion of Series B Preferred Stock into Common Stock in accordance with the provisions hereof, the Company covenants to list such Common Stock issuable upon conversion of the Series B Preferred Stock in accordance with the requirements of such exchange or automated quotation system at such time.

4. Taxes . The Company shall pay any and all transfer taxes that may be payable in respect of the issue or delivery of shares of Common Stock on conversion of Series B Preferred Stock. The Company shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issue and delivery of shares of Common Stock in a name other than that in which the Series B Preferred Stock so converted were registered, and no such issue or delivery shall be made unless and until the Person requesting such issue has paid to the Company the amount of any such tax, or has established to the satisfaction of the Company that such tax has been paid.

5. No Impairment . The Company will not by amendment of its Articles of Incorporation or through any or through any reorganization, recapitalization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be observed or performed hereunder by this corporation, but will at all times in good faith assist in the carrying out of all the provisions of this Articles of Amendment and in the taking of all such action as may be necessary or appropriate in order to protect the rights of the holders of the Series B Preferred Stock against impairment.

6. Fractional Shares. No fractional shares of Common Stock shall be issued upon conversion of Series B Preferred Stock but, in lieu of any fraction of a share of Common Stock which would otherwise be issuable in respect of the aggregate number of shares of Series B Preferred Stock so converted at one time by the same holder, the Company shall pay in cash an amount equal to the product of (i) the Closing Price of a share of Common Stock on the last Trading Day before the Mandatory Conversion Date and (ii) such fraction of a share of Common Stock otherwise issuable upon conversion of the shares of Series B Preferred Stock.

(g) Conversion Price Adjustments. The Conversion Price shall be adjusted from time to time (successively and for each event described) by the Company as follows:

1. In the event that the Company shall at any time or from time to time after the Original Issue Date (i) pay a dividend or make a distribution (other than a dividend or distribution paid or made to holders of shares of Series B Preferred Stock in the manner provided in Paragraph (d)(1) of this Section 10) on the outstanding shares of Common Stock in capital stock (which, for purposes of this Paragraph (g) shall include, without limitation, any options, warrants or other rights to acquire Capital Stock) of the Company, (ii) subdivide the outstanding shares of Common Stock into a larger number of shares, (iii) combine the outstanding shares of Common Stock into a smaller number of shares, (iv) issue any shares of its capital stock in a reclassification of the Common Stock or (v) pay a dividend or make a distribution (other than a dividend or distribution paid or made to holders of shares of Series B Preferred Stock in the manner provided in Paragraph (d)(1) of this Section 10) on the outstanding shares of Common Stock in securities of the Company pursuant to a shareholder rights plan, "poison pill" or similar arrangement, then, and in each such case, the Conversion Price in effect immediately prior to such event shall be increased or decreased, as applicable, (and any other appropriate actions shall be taken by the Company) so that the holder of any share of Series B Preferred Stock thereafter surrendered for conversion shall be entitled to receive the number of shares of Common Stock or other securities of the Company that such holder would have owned or would have been entitled to receive upon or by reason of any of the events described above, had such share of Series B Preferred Stock been converted immediately prior to the occurrence of such event (whether or not such holder of shares of Series B Preferred Stock had been eligible to convert its shares of Series B Preferred Stock on such date). An adjustment made pursuant to this Paragraph (g)(1) shall become effective retroactively (i) in the case of any such dividend or distribution, to a date immediately following the Close of Business on the Record Date for the determination of holders of Common Stock entitled to receive such dividend or distribution or (ii) in the case of any such subdivision, combination or reclassification, to the Close of Business on the day upon which such corporate action becomes effective.

2. In the event that the Company, at any time or from time to time after the Original Issue Date, shall take any action affecting its Common Stock similar to or having an effect similar to any of the actions described in Paragraph (g)(1) of this Section 10 (but not including any action described in any such Paragraph and without any duplication of any adjustments made pursuant to such Paragraphs) and the Board of Directors in good faith determines that it would be equitable in the circumstances to adjust the Conversion Price as a result of such action, then, and in each such case, the Conversion Price shall be decreased, if applicable, in such manner and at such time as the Board of Directors in good faith determines would be equitable in the circumstances (such determination to be evidenced in a resolution, a certified copy of which shall be sent to the holders of the Series B Preferred Stock). For the avoidance of doubt, in no event shall the Conversion Price be increased pursuant to the provisions of this Paragraph (g)(2).

3. Notwithstanding anything herein to the contrary, no adjustment under this Paragraph (g) need be made to the Conversion Price unless such adjustment is greater than one-tenth of one cent per share. Any lesser adjustment shall be carried forward and shall be made at the time of and together with the next subsequent adjustment, which, together with any adjustment or adjustments so carried forward, shall amount to an increase or decrease of at least 1% of such Conversion Price. Any adjustment to the Conversion Price carried forward and not theretofore made shall be made immediately prior to the conversion of any shares of Series B Preferred Stock pursuant to Paragraphs (f)(1) and (f)(2) of this Section 10.

(h) Redemption .

1. Election . At the written election (the " Series B Election ") of the holders of at least 62.5% of the then outstanding shares of Series B Preferred Stock made at any time on or after the fifth year anniversary of the Original Issue Date, the Company shall call for redemption, and shall redeem all, and not less than all, of the outstanding shares of Series B Preferred Stock on the date set forth in the Series B Election, provided that such date shall be at least 180 days after delivery to the Company of the Series B Election (the " Series B Redemption Date "), provided that if the Series B Redemption Date falls on a day other than a Business Day, the Series B Redemption Date shall be the next succeeding Business Day. The redemption price per share (the " Series B Redemption Price ") shall be equal to the greater of (x) the sum of (a) the Stated Value per share of the Series B Preferred Stock *plus* (b) an amount per share of Series B Preferred Stock equal to the accrued but unpaid dividends to which such holder of shares of Series B Preferred Stock is entitled to receive pursuant to Paragraph (f)(2) of this Section 10 to but excluding the date fixed for such redemption, if any, and (y) the product of (a) the Market Price per share of Common Stock and (b) the number of shares of Common Stock that such holder of Series B Preferred Stock would have been entitled to receive had it converted each such share of Series B Preferred Stock (whether or not such holder of Series B Preferred Stock had been eligible to convert its shares of Series B Preferred Stock on such Series B Redemption Date). For purposes of this Paragraph (h)(1), " Market Price " means the average Closing Price for the ten (10) consecutive Trading Days immediately preceding, but not including, the Redemption Date.

2. Notice of Redemption . Promptly following receipt of a Series B Election the Company shall provide written notice (the " Series B Redemption Notice ") to all holders of Series B Preferred Stock entitled to redemption under this Paragraph (h). Such Series B Redemption Notice shall set forth (i) the Series B Redemption Date and place of redemption; (ii) that all shares of Series B Preferred Stock held by such holder are to be redeemed; and (iii) the Series B Redemption Price.

3. Procedures . If, on or before the Series B Redemption Date, the funds necessary for such redemption shall have been set aside by the Company and deposited with a bank or trust company, in trust for the pro rata benefit of the holders of the Series B Preferred Stock, then, notwithstanding that any certificates for shares that have been called for redemption shall not have been surrendered for cancellation, the shares represented thereby shall no longer be deemed outstanding from and after such Series B Redemption Date, and all rights of holders of such shares so called for redemption shall forthwith, after such Series B Redemption Date, cease and terminate with respect to such shares, excepting only the right to receive the applicable Series B Redemption Price to which they are entitled.Any interest accrued on funds so deposited and unclaimed by shareholders entitled thereto shall be paid to such shareholders at the time their respective shares are redeemed or to the Company at the time unclaimed amounts are paid to it. In case any holder of Series B Preferred Stock shall not, within one (1) year after the final Series B Redemption Date, claim the amounts so deposited with respect to the redemption thereof, any such bank or trust company, shall, upon demand, pay over to the Company such unclaimed amounts and thereupon such bank or trust company shall be relieved of all responsibility in respect thereof to such holder and such holder shall look only to the Company for the payment thereof. Any funds so deposited with a bank or trust company which shall not be required for such redemption by reason of the exercise subsequent to the date of such deposit of the right of conversion of any shares or otherwise shall be returned to the Company forthwith.

4. Failure to Redeem . If the funds of the Company legally available for redemption of shares of Series B Preferred Stock on the Series B Redemption Date are insufficient to redeem the total number of shares of Series B Preferred Stock to be redeemed on such date, those funds which are legally available will be used to redeem the holders of the Series B Preferred Stock, ratably among the holders thereof in proportion to the redemption amounts otherwise payable to them, in the maximum amount of the Series B Redemption Price to which such holders of Series B Preferred Stock are entitled. The shares of Series B Preferred Stock not redeemed shall remain outstanding and entitled to all rights and preferences provided herein. At any time thereafter when additional funds of the Company are legally available for the redemption of such shares of Series B Preferred Stock, such funds will be used to redeem the remaining balance of any shares of Series B Preferred Stock that were required to be redeemed at the prior Series B Redemption Date. Notwithstanding anything to the contrary contained herein, interest shall accrue on any shares of Series B Preferred Stock required to be redeemed pursuant to this Paragraph (h) that have not been redeemed within thirty (30) days of the Series B Redemption Date at a rate of 15.0% per annum of the Series B Redemption Price from the Series B Redemption Date for so long as such shares remain outstanding.

5. Conversion Prior to Redemption . Notwithstanding the foregoing, if the Shareholder Approval is obtained prior to the Series B Redemption Date, whether or not a notice of Series B Election has been delivered to the Company, and whether or not the Company shall have previously sought, but failed to receive, the Shareholder Approval, the Series B shares shall be automatically converted into shares of Common Stock pursuant to and in accordance with Paragraph (f)(1) of this Section 10, and the Company shall have no obligation under this Paragraph (h) to redeem any shares of Series B Preferred Stock or any shares of Common Stock issued upon such conversion.

(i) Voting Rights; Information Rights .

1. The holders of shares of Series B Preferred Stock shall not be entitled to vote, except as otherwise provided in paragraphs (i)(2) and (i)(3) of this Section 10 or as otherwise required by applicable law.

2. For so long as at least 10% of the Series B Preferred Stock issued on the Original Issue Date remain outstanding, the Company shall not (by amendment, merger, consolidation or otherwise and either directly or through a subsidiary) without first obtaining the approval (by vote or written consent, as provided by law) of the holders of at least 62.5% of the then outstanding shares of Series B Preferred Stock, voting together as a single class:

(A) alter or change the rights, preferences, powers or privileges of the shares of Series B Preferred Stock pursuant to an amendment to the Articles of Incorporation or Bylaws or otherwise;

(B) increase or decrease (other than by conversion) the total number of authorized or issued shares of Series B Preferred Stock;

(C) authorize or issue, or obligate itself to issue, any equity security (including any other security convertible into or exercisable for any such equity security) having a preference over or on parity with the Series B Preferred Stock with respect to dividends or liquidation or amend the terms of any existing security to have a preference over or on parity with the Series B Preferred Stock with respect to dividends or liquidation ;

(D) redeem, purchase or otherwise acquire any shares of Junior Stock or any series of preferred stock other than the Series B Preferred Stock;

(E) declare, pay or set aside for payment any dividends on the Common Stock.

3. For so long as at least 10% of the Series B Preferred Stock issued on the Original Issue Date remain outstanding, the Company shall not (by amendment, merger, consolidation or otherwise and either directly or through a subsidiary) without first obtaining the approval (by vote or written consent, as provided by law) of the holders of at least a majority of the then outstanding shares of Series B Preferred Stock, voting together as a single class, effect a Deemed Liquidation Event, provided that the provisions of this paragraph (i)(3) shall expire, and no such approval of the Series B Preferred Stock shall be required with respect to the matters set forth in this paragraph (i)(3), from and after such time as the Original Holders no longer Beneficially Own at least a majority of the outstanding shares of Series B Preferred Stock.

4. Notwithstanding whether or not the Shareholder Approval shall have been obtained, the holders of shares of Series B Preferred Stock shall be entitled to notice of any shareholders' meeting delivered to the holders of Common Stock in accordance with the Bylaws and to otherwise receive all other notices and information made available or delivered by the Company to the holders of Common Stock.

(j) Record Holders . To the fullest extent permitted by applicable law, the Company may deem and treat the record holder of any share of Series B Preferred Stock as the true and lawful owner thereof for all purposes, and the Company shall not be affected by any notice to the contrary.

(k) Notices .

1. General . All notices or communications in respect of the Series B Preferred Stock shall be given to the holders of the Series B Preferred Stock in any manner permitted by the Depository Trust Company or any similar facility through which the Series B Preferred Stock is issued in book-entry form.

2. Notice of Certain Events . The Company shall, to the extent not included in the Exchange Act reports of the Company, provide reasonable written notice to each holder of the Series B Preferred Stock of any event the occurrence of which would result in an adjustment to the Conversion Price, including the then applicable Conversion Price.

(l) Other Rights . The shares of Series B Preferred Stock shall not have any rights, preferences, privileges or voting powers or relative, participating, optional or other special rights, or qualifications, limitations or restrictions thereof, other than as set forth herein or in the Articles of Incorporation or as provided by applicable law and regulation.

(m) Maturity . The Series B Preferred Stock shall be perpetual unless converted or redeemed in accordance with the terms of this Articles of Amendment.

(n) Replacement Certificates .

1. If physical certificates are issued, the Company shall replace any mutilated certificate at the holder's expense upon surrender of that certificate to the Company's transfer agent (the " Transfer Agent "). The Company shall replace certificates that become destroyed, stolen or lost at the holder's expense upon delivery to the Company and the Transfer Agent of satisfactory evidence that the certificate has been destroyed, stolen or lost, together with any indemnity that may be required by the Transfer Agent and the Company.

2. If physical certificates are issued, the Company shall not be required to issue any certificates representing the Series B Preferred Stock on or after the Mandatory Conversion Date. In place of the delivery of a replacement certificate following the Mandatory Conversion Date, the Transfer Agent, upon delivery of the evidence and indemnity described in clause (1) above, shall deliver the shares of Common Stock pursuant to the terms of the Series B Preferred Stock formerly evidenced by the certificate.

III.

The foregoing amendment was duly adopted by the Company's Board of Directors on December 1, 2010. No shareholder action was required.

INSMED INCORPORATED

Dated: December 1, 2010

By: /s/ Kevin P. Tully
Name: Kevin P. Tully
Title: Executive Vice President and Chief Financial Officer

ARTICLES OF AMENDMENT
TO THE
ARTICLES OF INCORPORATION, AS AMENDED,
of
INSMED INCORPORATED

I.

The name of the corporation is Insmed Incorporated (the " Company ").

II.

Article III of the Company's Articles of Incorporation, as amended, shall be amended by replacing the existing paragraph 8 with the following paragraph:

8. *Reverse Stock Split* . Simultaneously with the effective date of this amendment (the " Effective Time "), each 10 shares of the Company Common Stock, par value $0.01 per share, issued and outstanding immediately prior to the Effective Time (the " Old Common Stock ") shall, automatically and without any action on the part of the holder thereof, be reclassified as and changed, pursuant to a reverse stock split (the " Reverse Split "), into one share of the Company's outstanding Common Stock, par value $0.01 per share (the " New Common Stock "), subject to the treatment of fractional share interests as described below. Each holder of a certificate or certificates, which immediately prior to the Effective Time represented outstanding shares of Old Common Stock (the " Old Certificates "), shall be entitled to receive, upon surrender of such Old Certificates to the Company's transfer agent for cancellation, a certificate or certificates (the " New Certificates ") representing the number of whole shares of the New Common Stock into and for which the shares of the Old Common Stock formerly represented by such Old Certificates so surrendered are reclassified under the terms hereof. From and after the Effective Time, Old Certificates shall thereupon be deemed for all corporate purposes to evidence ownership of New Common Stock in the appropriately reduced whole number of shares. No certificates or scrip representing fractional share interests in New Common Stock will be issued, and no such fractional share interest will entitle the holder thereof to vote, or to any rights of a shareholder of the Company. In lieu of any fraction of a share of New Common Stock to which the holder would otherwise be entitled, the holder will receive a cash payment in U.S. dollars equal to such fraction multiplied by 10 times the average of the closing bid and ask price per share of Common Stock as quoted on the Nasdaq Capital Market for the five trading days immediately preceding the Effective Time. If more than one Old Certificate shall be surrendered at one time for the account of the same shareholder, the number of full shares of New Common Stock for which New Certificates shall be issued shall be computed on the basis of the aggregate number of shares represented by the Old Certificates so surrendered. In the event that the Company's transfer agent determines that a holder of Old Certificates has not surrendered all his, her or its certificates for exchange, the transfer agent shall carry forward any fractional share until all certificates of that holder have been presented for exchange such that payment for fractional shares to any one holder shall not exceed the value of one share. If any New Certificate is to be issued in a name other than that in which it was issued, the Old Certificates so surrendered shall be properly endorsed and otherwise in proper form for transfer, and the stock transfer tax stamps to the Old Certificates so surrendered shall be properly endorsed and otherwise in proper form for transfer, and the person or persons requesting such exchange shall affix any requisite stock transfer tax stamps to the Old Certificates surrendered, or provide funds for their purchase, or establish to the satisfaction of the transfer agent that such taxes are not payable. From and after the Effective Time, the amount of capital shall be represented by the shares of the New Common Stock into which and for which the shares of the Old Common Stock are reclassified, until thereafter reduced or increased in accordance with applicable law. All references elsewhere in the Articles of Incorporation, as amended, to the "Common Stock" shall, after the Effective Time, refer to the "New Common Stock."

III.

The amendment was proposed by the Board of Directors and submitted to the shareholders of the Company in accordance with Chapter 9 of Title 13.1 of the Code of Virginia. The designation, number of outstanding shares, and number of votes entitled to be cast by each voting group entitled to vote separately on the amendment are as follows:

Designation	Number of Outstanding Shares	Number of Votes
Common	156,537,341	156,537,341

The total number of undisputed votes cast for the amendment by each voting group was as follows:

Designation	Number of Undisputed Votes for the Amendment
Common	100,106,057

The number of votes cast for the amendment by each voting group was sufficient for approval by that voting group.

IV.

Pursuant to Section 13.1-606 of the Virginia Stock Corporation Act, the effective time and date of this Amendment to the Company's Articles of Incorporation, as amended, shall be 5:00 p.m., Eastern Standard Time, on March 2, 2011.

INSMED INCORPORATED

Dated: March 2, 2011

By: /s/ Kevin P. Tully
Name: Kevin P. Tully
Title: Executive Vice President & Chief Financial Officer

ARTICLES OF AMENDMENT
TO THE
ARTICLES OF INCORPORATION, AS AMENDED,
of
INSMED INCORPORATED
TO DELETE THE SERIES OF PREFERRED STOCK
DESIGNATED AS
SERIES B CONDITIONAL CONVERTIBLE PREFERRED STOCK

Pursuant to Section 13.1-639 of the Virginia Stock Corporation Act

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I.

The name of the corporation is Insmed Incorporated (the "Company").

II.

Pursuant to Section 13.1-639 of the Virginia Stock Corporation Act and the authority conferred upon the Board of Directors by the Articles of Incorporation, as amended, the Articles of Incorporation are hereby amended to delete in its entirety paragraph 10 of Article III of the Articles of Incorporation and all provisions thereof, which provisions were originally adopted by the Board of Directors to fix the preferences, limitations and rights of the series of shares of Preferred Stock designated therein as "Series B Conditional Convertible Preferred Stock" (none of which shares are outstanding as of the date hereof).

III.

The foregoing amendment was duly adopted by the Company's Board of Directors on June 12, 2012. No shareholder action was required.

INSMED INCORPORATED

Date: June 13, 2012

By: /s/ Kevin P. Tully
Name: Kevin P. Tully C.G.A.
Title: Executive Vice President & Chief Financial Officer

EXHIBIT 10.3

INSMED INCORPORATED

RESTRICTED UNIT AWARD AGREEMENT
UNDER THE AMENDED AND RESTATED
2000 STOCK INCENTIVE PLAN

Name of Grantee:

Number of Restricted Stock Units:

Grant Date:

Pursuant to the Insmed Incorporated Amended and Restated 2000 Stock Incentive Plan (the "Plan") as amended through the date hereof, Insmed Incorporated (the "Company") hereby grants an award of _____restricted stock units (the "Restricted Stock Units" or the "RSU Award") to the Grantee named above. The RSU Award shall be referred to herein as the "Award." Upon acceptance of this Award, the Grantee shall receive the number of Restricted Stock Units specified above, subject to the restrictions and conditions set forth herein and in the Plan.

If and to the extent that this Award Agreement conflicts or is inconsistent with the terms, conditions and provisions of any employment, consulting or similar services agreement between the Grantee and the Company as may be in effect (the "Service Agreement"), the Service Agreement shall control, and this Award Agreement shall be deemed to be modified accordingly so long as such modification is not expressly prohibited by the Plan.

The Company acknowledges the receipt from the Grantee of consideration with respect to the par value of the Stock in the form of cash, past or future services rendered to the Company by the Grantee or such other form of consideration as is acceptable to the Administrator.

1. Acceptance of Award . The Grantee shall have no rights with respect to this Award unless he or she shall have accepted this Award by signing and delivering to the Company a copy of this Award Agreement.

2. Restrictions and Conditions on Award . Restricted Stock Units granted herein may not be sold, assigned, transferred, pledged or otherwise encumbered or disposed of by the Grantee prior to vesting, and shall be subject to all the terms, conditions and restrictions set forth herein and in the Plan.

3. Timing and Form of Payout of Restricted Stock Units . As soon as practicable (but in no event later than 30 days) following the applicable Vesting Date, the vested Restricted Stock Units will be paid to the Grantee in a lump sum cash payment equal to the Fair Market Value of the shares of Stock underlying the Restricted Stock Units as of the applicable Vesting Date. Notwithstanding the foregoing, if, following the Grant Date, the shareholders of the Company approve an amendment to the Plan increasing the maximum aggregate number of shares of Stock that may be issued under the Plan to a number of shares of Stock sufficient to allow for the payment in full of the vested Restricted Stock Units in shares of Stock hereunder as well as under all other awards containing substantially similar terms and conditions as those set forth herein, then, at the Administrator's discretion, the vested Restricted Stock Units may be paid out in either (a) shares of Stock, (b) a cash payment equal to the Fair Market Value of the shares of Stock underlying the Restricted Stock Units as of the applicable Vesting Date, or (c) a combination of (a) and (b), as soon as practicable (but in no event later than 30 days) following the applicable Vesting Date.

4. Vesting of Award . The restrictions and conditions in Section 2 of this Agreement shall lapse on the date or dates specified in this Section 4, so long as the Grantee remains an employee of the Company or its Affiliates on such Vesting Date (defined below), subject to Section 6 below. Except as set forth in Section 5 below, the Award shall vest in accordance with the schedule set forth below.

Percentage of Award Vested	Vesting Date
33 1/3%	First Anniversary of the Grant Date
33 1/3%	Second Anniversary of the Grant Date
33 1/3%	Third Anniversary of the Grant Date

Except as otherwise provided in Sections 5 and 6 of this Agreement, the Grantee shall forfeit any unvested portion of the Award in the event the Grantee's employment is terminated prior to the Vesting Date.

Notwithstanding anything to the contrary herein or in the Plan, the Administrator may at any time accelerate the vesting schedule specified in this Section 4.

5. Change in Control . In the event of a Change in Control of the Company, fifty percent (50%) the unvested portion of the RSU Award, to the extent not previously forfeited or cancelled, shall immediately vest as of the date of such Change in Control.

6. Termination of Employment . Except as otherwise provided herein, any unvested portion of Award shall be forfeited without payment of consideration upon the termination of the Grantee's employment with the Company or its Affiliates for any reason, except as otherwise provided in the Section 6. Notwithstanding the foregoing, upon the Grantee's death (while an active employee of the Company or its Affiliates), the Award, to extent not previously forfeited or cancelled, shall immediately vest as of the date of the Grantee's death.

7. Voting Rights and Dividends . If and until such time as Restricted Stock Units are paid out in shares of Stock (if at all), the Grantee shall not have voting rights. However, all dividends and other distributions paid with respect to the Restricted Stock Units shall accrue and shall be converted to additional Restricted Stock Units based on the closing price of the Stock on the dividend distribution date. Such additional Restricted Stock Units shall be subject to the same restrictions on transferability as are the Restricted Stock Units with respect to which they were paid.

8. Change in Capital Structure . The terms of these Restricted Stock Units shall be adjusted as the Committee determines is equitably required in the event the Company effects one or more stock dividends, stock split-ups, subdivisions or consolidations of shares or other similar changes in capitalization.

9. Incorporation of Plan . Notwithstanding anything herein to the contrary, this Agreement shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section III of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein, provided that, as used herein, the term Administrator shall mean the Committee.

10. Transferability . This Agreement is personal to the Grantee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution.

11. Tax Withholding . The Grantee shall, not later than the date as of which the receipt of this Award becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event.

12. No Obligation to Continue Employment . Neither the Company nor any Affiliate is obligated by or as a result of the Plan or this Agreement to continue the Grantee in employment and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Affiliate to terminate the employment of the Grantee at any time.

13. Notices . Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

INSMED INCORPORATED

By: _____
Name: Andrew Drechsler
Title: Chief Financial Officer

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned.

Dated: _____

_____
Grantee's Signature

EXHIBIT 10.4

INSMED INCORPORATED

RESTRICTED UNIT AWARD AGREEMENT
UNDER THE AMENDED AND RESTATED
2000 STOCK INCENTIVE PLAN

Name of Grantee:

Number of Restricted Stock Units:

Grant Date:

Pursuant to the Insmed Incorporated Amended and Restated 2000 Stock Incentive Plan (the "Plan") as amended through the date hereof, Insmed Incorporated (the "Company") hereby grants an award of _____ restricted stock units (the "Restricted Stock Units" or the "RSU Award") to the Grantee named above. The RSU Award shall be referred to herein as the "Award." Upon acceptance of this Award, the Grantee shall receive the number of Restricted Stock Units specified above, subject to the restrictions and conditions set forth herein and in the Plan.

The Company acknowledges the receipt from the Grantee of consideration with respect to the par value of the Stock in the form of cash, past or future services rendered to the Company by the Grantee or such other form of consideration as is acceptable to the Administrator.

1. Acceptance of Award . The Grantee shall have no rights with respect to this Award unless he or she shall have accepted this Award by signing and delivering to the Company a copy of this Award Agreement.

2. Restrictions and Conditions on Award . Restricted Stock Units granted herein may not be sold, assigned, transferred, pledged or otherwise encumbered or disposed of by the Grantee prior to vesting, and shall be subject to all the terms, conditions and restrictions set forth herein and in the Plan.

3. Timing and Form of Payout of Restricted Stock Units . As soon as practicable (but in no event later than 30 days) following the applicable Vesting Date, the vested Restricted Stock Units at the Administrator's discretion, may be paid out in either (a) shares of Stock or (b) a cash payment equal to the Fair Market Value of the shares of Stock underlying the Restricted Stock Units.

4. Vesting of Award . Except as set forth in Section 5 of this Agreement, the restrictions and conditions in Section 2 of this Agreement shall lapse, with respect to 100% of the RSU Award, on the first anniversary of the Grant Date (the "Vesting Date") so long as (a) the Grantee remains a member of the board of directors of the Company or its Affiliates on such Vesting Date and (b) the Grantee attends at least seventy-five percent (75%) of the board of directors meetings that take place during the period of time commencing from the Grant Date and ending of the first anniversary of the Grant Date.

Except as otherwise provided in Sections 5 and 6 of this Agreement, the Grantee shall forfeit any unvested portion of the RSU Award if either the following shall occur: (i) in the event the Grantee's service as a member of the board of directors of the Company or its Affiliates is terminated for any reason prior to the Vesting Date; or (ii) in the event that the Grantee fails to attend at least seventy-five percent (75%) of the board of directors meetings that take place during the period of time commencing from the Grant Date and ending of the first anniversary of the Grant Date.

Notwithstanding anything to the contrary herein or in the Plan, the Administrator may at any time accelerate the vesting schedule specified in this Section 4.

5. Change in Control . In the event of a Change in Control of the Company, the unvested portion of the RSU Award, to the extent not previously forfeited or cancelled, shall immediately vest as of the date of such Change in Control.

6. Termination of Service . Except as otherwise provided herein, any unvested portion of the RSU Award shall be forfeited without payment of consideration upon the termination of the Grantee's service with the Company or its Affiliates for any reason, except as otherwise provided in this Section 6. Notwithstanding the foregoing, upon the Grantee's death (while an active director of the board of the Company or its Affiliates) or upon the termination of the Grantee's service due to Disability (as defined below), the RSU Award to extent not previously forfeited or cancelled, shall immediately vest as of the date of the Grantee's death or Disability. For purposes of this Agreement, the Grantee will be considered "disabled" if, as a result of the Grantee's incapacity due to physical or mental illness, the Grantee shall have been absent from his duties to the Company or its Affiliates on a full-time basis for 180 calendar days in the aggregate in any 12-month period.

7. Voting Rights and Dividends . If and until such time as Restricted Stock Units are paid out in shares of Stock (if at all), the Grantee shall not have voting rights. However, all dividends and other distributions paid with respect to the Restricted Stock Units shall accrue and shall be converted to additional Restricted Stock Units based on the closing price of the Stock on the dividend distribution date. Such additional Restricted Stock Units shall be subject to the same restrictions on transferability as are the Restricted Stock Units with respect to which they were paid.

8. Change in Capital Structure . The terms of these Restricted Stock Units shall be adjusted as the Committee determines is equitably required in the event the Company effects one or more stock dividends, stock split-ups, subdivisions or consolidations of shares or other similar changes in capitalization.

9. Incorporation of Plan . Notwithstanding anything herein to the contrary, this Agreement shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section III of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein, provided that, as used herein, the term Administrator shall mean the Committee.

10. Transferability . This Agreement is personal to the Grantee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution.

11. Tax Withholding . The Grantee shall, not later than the date as of which the receipt of this Award becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event.

12. No Obligation to Continue Service . Neither the Company nor any Affiliate is obligated by or as a result of the Plan or this Agreement to continue the Grantee's services and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Affiliate to terminate the services of the Grantee at any time.

13. Notices . Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

INSMED INCORPORATED

By: _____
Name: Andrew Drechsler
Title: Chief Financial Officer

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned.

Dated: _____ _____

EXHIBIT 10.5

INSMED INCORPORATED

INCENTIVE STOCK OPTION AGREEMENT

No. of shares subject to Option: _____

THIS Incentive Stock Option Agreement ("Agreement") dated this _____, between Insmed, Incorporated, a Virginia corporation (the "Company"), and _____ ("Participant"), is made pursuant and subject to the provisions of the Insmed Incorporated 2000 Stock Incentive Plan, as amended (the "Plan"), a copy of which has been made available to the Participant. All terms used herein that are defined in the Plan have the same meaning given them in the Plan.

If and to the extent that this Agreement conflicts or is inconsistent with the terms, conditions and provisions of any employment, consulting or similar services agreement between the Participant and the Company as may be in effect (the "Service Agreement"), the Service Agreement shall control, and this Award Agreement shall be deemed to be modified accordingly so long as such modification is not expressly prohibited by the Plan.

1. **Grant of Option**. Pursuant to the Plan, the Company, on _____ (the "Date of Grant"), granted to Participant, subject to the terms and conditions of the Plan and subject further to the terms and conditions herein set forth, the right and option to purchase from the Company all or any part of an aggregate of _____ shares of Common Stock at the option price of $_____ per share, being not less than the Fair Market Value of such shares on the Date of Grant ("Option"). This Option is intended to be an "incentive stock option" within the meaning of Section 422 of the Code. This Option is exercisable as hereinafter provided.

2. **Terms and Conditions**. This Option is subject to the following terms and conditions:

(a) **Expiration Date**. This Option shall expire ten years from the Date of Grant (the "Expiration Date").

(b) **Exercise of Option**. Except as provided in paragraphs 3, 4 and 5, this Option shall be exercisable with respect to twenty-five percent (25%) of the shares of Common Stock subject to this Option on the first anniversary of the Date of Grant (the "First Anniversary Date") and with respect to an additional twelve and a half percent (12.5%) of the shares of Common Stock subject to this Option on the sixth month anniversary of the First Anniversary Date and each sixth month anniversary date thereafter through the fourth anniversary of the Date of Grant. If the foregoing schedule would produce fractional shares, the number of shares for which the Option becomes exercisable shall be rounded down to the nearest whole share. Once this Option has become exercisable in accordance with the preceding sentence it shall continue to be exercisable until the termination of Participant's rights hereunder pursuant to paragraph 3, 4 or 5 or until the Option has expired pursuant to subparagraph 2(a). A partial exercise of this Option shall not affect Participant's right to exercise this Option with respect to the remaining shares, subject to the conditions of the Plan and this Agreement.

(c) **Method of Exercising Option and Payment for Shares** . This Option shall be exercised by written notice delivered to the attention of the Company's Principal Financial Officer at the Company's principal office in New Jersey (see attachment A – "Notice of Option Exercise"). The exercise date shall be (i) in the case of notice by mail, the date of postmark, or (ii) if delivered in person, the date of delivery. Such notice shall be accompanied by payment of the Option price in full, in cash or cash equivalent acceptable to the Committee, or by the surrender of shares of Common Stock with an aggregate Fair Market Value (determined as of the day preceding the exercise date) which, together with any cash or cash equivalent paid, is not less than the Option price for the number of shares for which this Option is being exercised.

(d) **Nontransferability** . This Option may not be transferred except by will or by the laws of descent and distribution. During Participant's lifetime, this Option may be exercised only by Participant.

(e) **Acceptance of Option.** The Participant shall have no rights with respect to this Option unless he or she shall have accepted this Option by signing and delivering to the Company a copy of this Agreement within thirty (30) days of the Agreement date set forth in the first paragraph of this Agreement.

3. **Exercise in the Event of Death** . In the event Participant dies before the expiration of this Option pursuant to subparagraph 2(a), this Option shall be exercisable with respect to all or part of the shares of Common Stock that Participant was entitled to purchase under subparagraph 2(b) on the date of Participant's death. In that event, this Option may be exercised, to the extent exercisable under subparagraph 2(b), by Participant's estate or by the person or persons to whom his rights under this Option shall pass by will or the laws of descent and distribution. Participant's estate or such persons may exercise this Option within one (1) year of Participant's death or during the remainder of the period preceding the Expiration Date, whichever is shorter.

4. **Exercise in the Event of Permanent and Total Disability** . In the event Participant becomes permanently and totally disabled within the meaning of Section 22(e)(3) of the Code ("Permanently and Totally Disabled") before the expiration of this Option pursuant to subparagraph 2(a), this Option shall be exercisable with respect to all or part of the shares of Common Stock that Participant was entitled to purchase under subparagraph 2(b) on the date he ceases to be employed by the Company and its Affiliates as a result of his becoming Permanently and Totally Disabled. In that event, Participant may exercise this Option, to the extent exercisable under subparagraph 2(b), within one (1) year of the date he ceases to be employed by the Company and its Affiliates as a result of his becoming Permanently and Totally Disabled or during the period preceding the Expiration Date, whichever is shorter.

5. **Exercise After Termination of Employment .** Except as provided in paragraphs 3 and 4 hereof, if the Participant ceases to be employed by the Company and its Affiliates prior to the Expiration Date, this Option shall be exercisable for all or part of the number of shares that the Participant was entitled to purchase under subparagraph 2(b), as well as set forth under any Service Agreement, on the date of Participant's termination of employment. In that event, Participant may exercise this Option, to the extent exercisable under subparagraph 2(b) and/or under any Service Agreement, during the remainder of the period preceding the Expiration Date or until the date that is three (3) months after the date he ceases to be employed by the Company and its Affiliates, whichever is shorter.

6. **Notice**. Any notice or other communication given pursuant to this Agreement shall be in writing and shall be personally delivered or mailed by United States registered or certified mail, postage prepaid, return receipt requested, to the Company at its principal place of business or to the Participant at the address on the payroll records of the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing. Any such notice shall be deemed to have been given (a) on the date of postmark, in the case of notice by mail, or (b) on the date of delivery, if delivered in person.

7. **Fractional Shares**. Fractional shares shall not be issuable hereunder, and when any provision hereof may entitle Participant to a fractional share such fraction shall be disregarded.

8. **No Right to Continued Employment**. This Option does not confer upon Participant any right to continue in the employ of the Company or an Affiliate, nor shall it interfere in any way with the right of the Company or an Affiliate to terminate such employment at any time.

9. **Change in Capital Structure**. The terms of this Option shall be adjusted as the Committee determines is equitably required in the event the Company effects one or more stock dividends, stock split-ups, subdivisions or consolidations of shares or other similar changes in capitalization.

10. **Governing Law**. This Agreement shall be governed by the laws of the Commonwealth of Virginia.

11. **Conflicts**. In the event of any conflict between the provisions of the Plan as in effect on the date hereof and the provisions of this Agreement, the provisions of the Plan shall govern. All references herein to the Plan shall mean the Plan as in effect on the date hereof.

12. **Participant Bound by Plan**. Participant hereby acknowledges receipt of a copy of the Plan and agrees to be bound by all the terms and provisions thereof.

13. **Binding Effect**. Subject to the limitations stated above and in the Plan, this Agreement shall be binding upon and inure to the benefit of the legatees, distributees, and personal representatives of Participant and the successors of the Company.

14. **Incentive Stock Option Treatment**. The terms of this Option shall be interpreted in a manner consistent with the intent of the Company and the Participant that the Option qualify as an Incentive Stock Option under Section 422 of the Code. If any provision of the Plan or this Agreement shall be impermissible in order for the Option to qualify as an Incentive Stock Option, then the Option shall be construed and enforced as if such provision had never been included in the Plan or the Option. If and to the extent that the number of Options granted pursuant to this Agreement exceeds the limitations contained in Section 422 of the Code on the value of Shares with respect to which this Option may qualify as an Incentive Stock Option, this Option shall be a Non-Qualified Stock Option.

[Signatures on Following Page]

IN WITNESS WHEREOF, the Company has caused this Agreement to be signed by a duly authorized officer, and Participant has affixed his signature hereto.

INSMED INCORPORATED

By: _____
Name: Will Lewis
Title: CEO and President

_____
[NAME OF PARTICIPANT]

Attachment A

Chief Financial Officer
Insmed Incorporated
9 Deer Park Drive, Suite C
Monmouth Junction, NJ 08852-1919

Notice Of Option Exercise

This letter is notice of my decision to exercise the option that was granted to me on _____. The exercise will be effective on _____. I am exercising the option for _____ shares of Common Stock. Enclosed is my check for $ _____, which is the aggregate option price for the number of shares for which I am exercising the option.

Please issue the certificate according to the following instructions:

Name/entity stock certificate issued to:
(If entity is a trust, please include date trust was established.) _____

Address to send stock certificate: _____
_____
_____

Sincerely,

_____

Accepted by: _____

Date: _____

Note : The date of exercise cannot be earlier than the date of delivery of this notice or the postmark, if the notice is mailed.

EXHIBIT 10.6

INSMED INCORPORATED

NON-QUALIFIED STOCK OPTION AGREEMENT

No. of shares subject to Option: _____

THIS AGREEMENT dated this _____, between INSMED INCORPORATED, a Virginia corporation (the "Company"), and _____ ("Participant"), is made pursuant and subject to the provisions of the Insmed Incorporated 2000 Stock Incentive Plan, as amended (the "Plan"), a copy of which has been made available to the Participant. All terms used herein that are defined in the Plan have the same meaning given them in the Plan.

If and to the extent that this Agreement conflicts or is inconsistent with the terms, conditions and provisions of any employment, consulting or similar services agreement between the Participant and the Company as may be in effect (the "Service Agreement"), the Service Agreement shall control, and this Award Agreement shall be deemed to be modified accordingly so long as such modification is not expressly prohibited by the Plan.

1. **Grant of Option** . Pursuant to the Plan, the Company, on _____ (the "Date of Grant"), granted to Participant, subject to the terms and conditions of the Plan and subject further to the terms and conditions herein set forth, the right and Option to purchase from the Company all or any part of an aggregate of _____ shares of Common Stock at the Option price of $_____ per share, being not less than the Fair Market Value of such shares on the Date of Grant. This Option is intended to be a nonqualified stock option and not an "incentive stock option" within the meaning of Section 422 of the Code. This Option is exercisable as hereinafter provided.

2. **Terms and Conditions** . This Option is subject to the following terms and conditions:

(a) **Expiration Date** . This Option shall expire ten years from the Date of Grant (the "Expiration Date").

(b) **Exercise of Option** . Except as provided in paragraphs 3, 4 and 5, this Option shall be exercisable with respect to twenty-five percent (25%) of the shares of Common Stock subject to this Option on the first anniversary of the Date of Grant (the "First Anniversary Date") and with respect to an additional twelve and a half percent (12.5%) of the shares of Common Stock subject to this Option on the sixth month anniversary of the First Anniversary Date and each sixth month anniversary date thereafter through the fourth anniversary of the Date of Grant. If the foregoing schedule would produce fractional shares, the number of shares for which the Option becomes exercisable shall be rounded down to the nearest whole share. Once this Option has become exercisable in accordance with the preceding sentence it shall continue to be exercisable until the termination of Participant's rights hereunder pursuant to paragraph 3, 4 or 5 or until the Option has expired pursuant to subparagraph 2(a). A partial exercise of this Option shall not affect Participant's right to exercise this Option with respect to the remaining shares, subject to the conditions of the Plan and this Agreement.

(c) **Method of Exercising Option and Payment for Shares** . This Option shall be exercised by written notice delivered to the attention of the Company's Principal Financial Officer at the Company's principal office in New Jersey (see attachment A – "Notice of Option Exercise"). The exercise date shall be (i) in the case of notice by mail, the date of postmark, or (ii) if delivered in person, the date of delivery. Such notice shall be accompanied by payment of the Option price in full, in cash or cash equivalent acceptable to the Committee, or by the surrender of shares of Common Stock with an aggregate Fair Market Value (determined as of the day preceding the exercise date) which, together with any cash or cash equivalent paid, is not less than the Option price for the number of shares for which this Option is being exercised.

(d) **Nontransferability** . This Option may not be transferred except by will or by the laws of descent and distribution. During Participant's lifetime, this Option may be exercised only by Participant.

3. **Exercise in the Event of Death** . In the event Participant dies before the expiration of this Option pursuant to subparagraph 2(a), this Option shall be exercisable with respect to all or part of the shares of Common Stock that Participant was entitled to purchase under subparagraph 2(b) on the date of Participant's death. In that event, this Option may be exercised, to the extent exercisable under subparagraph 2(b), by Participant's estate or by the person or persons to whom his rights under this Option shall pass by will or the laws of descent and distribution. Participant's estate or such persons may exercise this Option within one (1) year of Participant's death or during the remainder of the period preceding the Expiration Date, whichever is shorter.

4. **Exercise in the Event of Permanent and Total Disability** . In the event Participant becomes permanently and totally disabled within the meaning of Section 22(e)(3) of the Code ("Permanently and Totally Disabled") before the expiration of this Option pursuant to subparagraph 2(a), this Option shall be exercisable with respect to all or part of the shares of Common Stock that Participant was entitled to purchase under subparagraph 2(b) on the date he ceases to be employed by the Company and its Affiliates as a result of his becoming Permanently and Totally Disabled. In that event, Participant may exercise this Option, to the extent exercisable under subparagraph 2(b), within one (1) year of the date he ceases to be employed by the Company and its Affiliates as a result of his becoming Permanently and Totally Disabled or during the period preceding the Expiration Date, whichever is shorter.

5. **Exercise After Termination of Employment .** Except as provided in paragraphs 3 and 4 hereof, if the Participant ceases to be employed by the Company and its Affiliates prior to the Expiration Date, this Option shall be exercisable for all or part of the number of shares that the Participant was entitled to purchase under subparagraph 2(b), as well as set forth under any Service Agreement, on the date of Participant's termination of employment. In that event, Participant may exercise this Option, to the extent exercisable under subparagraph 2(b) and/or under Service Agreement, during the remainder of the period preceding the Expiration Date or until the date that is three (3) months after the date he ceases to be employed by the Company and its Affiliates, whichever is shorter.

6. **Notice** . Any notice or other communication given pursuant to this Agreement shall be in writing and shall be personally delivered or mailed by United States registered or certified mail, postage prepaid, return receipt requested, to the Company at its principal place of business or to the Participant at the address on the payroll records of the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing. Any such notice shall be deemed to have been given (a) on the date of postmark, in the case of notice by mail, or (b) on the date of delivery, if delivered in person.

7. **Fractional Shares**. Fractional shares shall not be issuable hereunder, and when any provision hereof may entitle Participant to a fractional share such fraction shall be disregarded.

8. **No Right to Continued Employment**. This Option does not confer upon Participant any right to continue in the employ of the Company or an Affiliate, nor shall it interfere in any way with the right of the Company or an Affiliate to terminate such employment at any time.

9. **Change in Capital Structure**. The terms of this Option shall be adjusted as the Committee determines is equitably required in the event the Company effects one or more stock dividends, stock split-ups, subdivisions or consolidations of shares or other similar changes in capitalization.

10. **Governing Law**. This Agreement shall be governed by the laws of the Commonwealth of Virginia.

11. **Conflicts**. In the event of any conflict between the provisions of the Plan as in effect on the date hereof and the provisions of this Agreement, the provisions of the Plan shall govern. All references herein to the Plan shall mean the Plan as in effect on the date hereof.

12. **Participant Bound by Plan**. Participant hereby acknowledges receipt of a copy of the Plan and agrees to be bound by all the terms and provisions thereof.

13. **Binding Effect**. Subject to the limitations stated above and in the Plan, this Agreement shall be binding upon and inure to the benefit of the legatees, distributees, and personal representatives of Participant and the successors of the Company.

IN WITNESS WHEREOF, the Company has caused this Agreement to be signed by a duly authorized officer, and Participant has affixed his signature hereto.

INSMED INCORPORATED

By: _____
Name: Will Lewis
Title: CEO and President

_____
[NAME OF PARTICIPANT]

Attachment A

Chief Financial Officer
Insmed Incorporated
9 Deer Park Drive, Suite C
Monmouth Junction, NJ 08852-1919

Notice Of Option Exercise

This letter is notice of my decision to exercise the option that was granted to me on _____. The exercise will be effective on _____. I am exercising the option for _____ shares of Common Stock. Enclosed is my check for $ _____, which is the aggregate option price for the number of shares for which I am exercising the option.

Please issue the certificate according to the following instructions:

Name/entity stock certificate issued to:
(If entity is a trust, please include date trust was established.) _____

Address to send stock certificate: _____
_____
_____

Sincerely,

_____

Accepted by: _____

Date: _____

Note : The date of exercise cannot be earlier than the date of delivery of this notice or the postmark, if the notice is mailed.

Pursuant to 17 CFR 240.24b-2, confidential information (indicated by [***]) has been omitted from Exhibit 10.22 and has been filed separately with the Securities and Exchange Commission pursuant to a Confidential Treatment Application filed with the Commission.

EX-10.22

LICENSE AGREEMENT

This License Agreement (this " **Agreement** ") effective as of the 25th day of April, 2008 (" **Effective Date** "), is 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 with registered offices at 11 Deer Park Drive, Suite 117, Monmouth Jct., NJ 08852, United States of America (" **Transave** "). Each of PARI and Transave shall be referred to as a " **Party** ," and collectively the " **Parties** ."

RECITALS

WHEREAS, Transave has acquired, developed and produced certain technology and formulation rights commonly referred to as Arikace™, a proprietary amikacin antibiotic based on Transave's proprietary sustained release liposomal technology for inhalation, for the treatment and prevention of Pseudomonas aeruginosa infection in patients with cystic fibrosis and bronchiectasis;

WHEREAS, PARI is in the business of developing and commercializing drug nebulizer devices and drug formulation methodologies, and PARI has developed a drug nebulizer device;

WHEREAS, PARI and Transave have entered into a Clinical Supply Agreement effective the 4 th day of April 2007 (the **"Clinical Supply Agreement"**);

WHEREAS, Pari GmbH and Transave entered into a Feasibility Study Agreement dated the 10 th day of January 2007, which was assigned and transferred to PARI on the 27 th of March 2007 (**"Feasibility Agreement"**);

WHEREAS, PARI and Transave executed a Statement of Work No. 3 for the Feasibility Agreement on the 26 th day of October 2007 (**"Feasibility Statement of Work No. 3"**);

WHEREAS, Transave desires to use a PARI drug nebulizer device for aerosolizing Arikace for pulmonary delivery, and PARI desires to optimize its drug nebulizer device for aerosolizing Transave's Arikace for pulmonary delivery; and

WHEREAS, PARI desires to perform evaluation, research and development activities with Transave related to PARI's nebulizer device technology, and Transave desires to pay PARI for such activities and to obtain a license to certain PARI intellectual property rights in connection with the development and commercialization of Arikace with an optimized PARI nebulizer device, all on the terms and conditions set forth herein.

AGREEMENT

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, PARI and Transave agree as follows:

Article 1 – Definition s

As used in this Agreement, the following terms shall have the following meanings while other terms may be defined parenthetically throughout this Agreement:

1.1 " **Affiliate(s)** " of a Party means any person or entity that directly or indirectly owns or controls, is owned or controlled by or is under common control with such Party, in each case, only for so long as such control exists. As used in this definition only, "control" of an entity means beneficial ownership, directly or indirectly, of fifty percent (50%) or more of the outstanding voting shares or securities or the ability otherwise to elect or appoint a majority of the board of directors or other managing authority of such entity.

1.2 [***]

1.3 " **Applicable Laws and Standards** " means (a) all laws, ordinances, rules, directives and regulations applicable to the Products, the Project or this Agreement, including without limitation applicable local laws and regulations in each country in the Transave Territory, (b) applicable regulations and guidelines of the FDA and other Regulatory Authorities and the ICH guidelines; (c) as applicable to the particular activities performed, Good Manufacturing Practices, Good Laboratory Practices and Good Clinical Practices promulgated by the FDA and other Regulatory Authorities or the ICH; and (d) all applicable industry and trade standards, including the applicable standards of the International Organization for Standardization (ISO).

1.4 " **Arikace** " means Transave's proprietary amikacin antibiotic (including the 70 mg/ml formulation) based on Transave's proprietary sustained release liposomal technology for inhalation.

1.5 " **Billable-hour** " means an hour of activities performed by or on behalf of PARI, but excluding: non-work time and time spent on traveling, training, information technology support or laboratory technical support, administrative or facilities support, time entry, finance, legal, human resources or purely clerical activities, or other support functions not directly requested by Transave.

1.6 " **Commercially Reasonable Efforts** " means those commercially reasonable efforts customarily used by companies in the biopharmaceutical industry (with respect to Transave) and the biomedical device industry (with respect to PARI) for carrying out in a sustained manner a particular task or obligation, and at least equivalent to those level of efforts applied by a Party for its other priority products.

1.7 **"Competing Nebulizer"** shall mean any Nebulizer which has the performance specification feature set forth below for a single treatment, including any Device or eFlow but excluding the [***], [***] and the [***] devices:

[***]

[***]

1.8 " **Confidential Information** " shall have the meaning given to it in Section 11.1.

1.9 " **Control** " means, with respect to an item of information or intellectual property rights, possession by such Party of the power and authority, whether arising by ownership, license, or other authorization, to disclose such item as required by this Agreement, and/or to grant and authorize licenses or sublicenses under such items that are within the scope granted to the other Party under this Agreement.

1.10 " **Covered** " means with respect to a product that (a) such product or its manufacture, use, sale, offer for sale, importation or exportation would infringe a Valid Claim of a Patent Right within the Intellectual Property, in the country of such manufacture, use, sale, offer for sale, importation or exportation, or (b) such product incorporates or is made using material Know-how within such Intellectual Property.

1.11 " **Data** " means all data, data sets, test data, pre-clinical and clinical trial data, analyses, reports, regulatory filings and approvals and the information therein or associated therewith (including drug master files and device master files, supporting data, regulatory correspondence and meeting minutes) and rights to reference the same, in each case:

(a) that are generated by either Party in the course of performance pursuant to a Work Plan or under this Agreement (" **Project Data** ");

(b) that are owned or controlled by PARI prior to the Effective Date, or generated by PARI during the term of this Agreement outside of performing the Work Plans, and are necessary or useful for the efforts of Transave, its Affiliates or Sublicensees in obtaining Marketing Approval for the Device (" **Existing PARI Data** "); or

(c) that are owned or controlled by Transave prior to the Effective Date, or generated by Transave during the term of this Agreement, and are necessary or useful for the efforts of PARI in performing the Work Plan(s) or in obtaining Marketing Approval for the Device but excluding any Data related to the Project Intellectual Property (" **Existing Transave Data** ").

1.12 " **Device** " means the eFlow (including the following components: control unit with screen, nebulizer handset with aerosol head, nebulizer connection cord and power supply) that is based on the Present Device, that is to be optimized or developed for use with the Drug Product, and that otherwise at least meets the Specifications, as defined below and recited in Exhibit 1.38 for a single treatment, but specifically excluded from the foregoing are the [***], [***] and [***] devices. The Parties acknowledge and agree that until the Device is finalized in accordance with this Agreement, the Present Device shall be used by the Parties hereunder for research, development and testing efforts related to this Agreement.

1.13 **"Device Accessories"** means those types of accessories sold by PARI as of the Effective Date or during the term of this Agreement for use with Devices, which are not specific to the drug substance being delivered by such Devices, including *e.g.* power adapters, carrying cases, face masks, and any replacement parts associated with the foregoing.

1.14 " **Drug Product** " means an Arikace pharmaceutical preparation that is formulated for delivery via pulmonary administration exclusively for use with the Device in the Transave Field.

1.15 **"eFlow"** shall mean the Nebulizer proprietary to PARI or its Affiliates that is based on perforated vibrating membrane technology and includes the mixing chamber and valve system associated with the device that is currently sold under the tradename EFLOW ® .

1.16 [***]

1.17 " **Expired** ", " **Expiration** " or " **Expiry** " means expired, lapsed, been canceled or become abandoned and has not been finally found to be invalid (or not valid) or unenforceable by an unreversable or unappealable (or for which no appeal has been timely filed) final decision or judgment of a court or other authority or agency of competent jurisdiction.

1.18 " **Exploit** " or " **Exploitation** " means to formulate, research, test, develop, seek regulatory approval for, make, have made, use, sell, have sold, offer for sale, market, promote, import, export, display, distribute or otherwise commercialize or dispose of.

1.19 " **FDA** " means the United States Food and Drug Administration or any successor to that agency.

1.20 " **First Commercial Sale** " means the first commercial sale of a Drug Product subject to royalties under Article 6, by or under authority of Transave, its Affiliates and/or their Sublicensees in a country in the Transave Territory, after Marketing Approval in such country has been obtained.

1.21 " **GAAP** " means generally accepted accounting principles in the United States or Germany, or the International Accounting Standard, consistently applied by a Party throughout its enterprise.

1.22 " **Good Manufacturing Practices** ," or " **GMP** " means all good manufacturing practices as promulgated by the Regulatory Authority of the country where the Device is being sold, in the form of laws or regulations or guidance documents, for the manufacturing of pharmaceutical products, including in the United States as promulgated by the FDA 21 CFR §§ 210-211, and medical devices, including 21 CFR § 820 – Quality System Regulation.

1.23 " **GMP Manufacturing** " means all processes and activities typically engaged in by a person or entity in the pharmaceutical or medical device industry for the GMP manufacture of a product or component thereof, including procuring raw materials, manufacturing, quality control and assurance testing, GMP record keeping, packaging and labeling.

1.24 " **Improvement** " means any improvements, modifications, discoveries, inventions, developments, enhancements, derivative works, including the technology, Know-how and other intellectual property rights associated therewith, whether or not patentable or registrable or otherwise protectable, in each case with respect to the Device or any other eFlow.

1.25 **"Initiation** " of a clinical trial means the first dosing of the first human patient in such trial.

1.26 " **Intellectual Property** " means (a) any of the following, whether existing now or in the future anywhere in the world: patents, inventor's certificates, registrations and applications therefor, including any provisionals, additions, divisionals, continuations, substitutions, continuations-in-part, together with re-examinations, reissues, renewals or extensions thereof and all foreign counterparts of any of the foregoing (collectively, " **Patent Rights** "), and (b) all Data, ideas, pharmaceutical, chemical and biological materials, products and compositions, tests, assays, techniques, methods, procedures, technical and non-technical data and other information relating to any of the foregoing, drawings, plans, designs, diagrams, sketches, specifications or other documents containing such information or materials, and business processes, price data and information, marketing data and information, sales data and information, marketing plans and market research (collectively, " **Know-how** "). It is understood, however, that Know-how does not include information that falls within exceptions of the definition of "Confidential Information" set forth in Section 11.1 of this Agreement. Intellectual Property includes all enforcement rights.

1.27 " **MAA** " means a fully completed marketing authorization application (filed with the FDA, if in the United States or to the counterpart of the FDA if outside the United States), including all supporting documentation and data required for such application to be accepted for substantive review, filed with a Regulatory Authority to seek Marketing Approval for a particular indication in a particular country. It is understood that MAA does not include applications for pricing or reimbursement approval.

1.28 " **Major EU Countries** " means Germany, France, UK, Italy and Spain.

1.29 " **Marketing Approval** " means all approvals, registrations or authorizations of any governmental entity that are necessary for the manufacturing, use, storage, import, transport and sale of products in a regulatory jurisdiction.

1.30 **"Most Recent Qualified Financing"** means, as of any given date, the most recent preferred stock financing of Transave which establishes an arms-length valuation for the shares of preferred stock issued in such financing and pursuant to which purchasers have purchased, or have committed to purchase, preferred stock of Transave with an aggregate purchase price of at least [***]. As of the date of this Agreement, the Most Recent Qualified Financing is the sale of Series D Convertible Preferred Stock of Transave pursuant to that certain Series D Convertible Preferred Stock Purchase Agreement, dated as of December 14, 2007 (as amended), by and among Transave and the Purchasers named therein.

1.31 **"Nebulizer"** shall mean any nebulizer or other device that delivers a formulation in the form of droplets to the airways, including the Device, any Competing Nebulizer and eFlow. For the avoidance of doubt, the term "Nebulizer" shall not include any device that delivers a formulation solely or primarily via a nasal route of administration.

1.32 " **Net Sales** " means the gross amounts received by Transave, its Affiliates and its permitted Sublicensees for their sales of Drug Product for use with a Device to third parties less the following deductions: (a) trade, wholesale, quantity, cash or other discounts, refunds, returns, rebates, credits and allowances to the extent actually taken; (b) import, export, excise, sales or use taxes, value added taxes, and other taxes, tariffs and duties imposed on such sales and actually paid by Transave, its Affiliates or permitted Sublicensees, as applicable; (c) out-bound packaging, handling, transportation, freight and freight insurance to the extent actually paid; (d) rebates, allowances or credits mandated by any government; (e) reimbursements, credits or chargebacks actually granted, allowed or incurred in the ordinary course of business (including any credits, volume rebates, charge-back and prime vendor rebates, reimbursements or similar payments granted or given to wholesalers and other distributors, buying groups, health care insurance carriers, pharmacy benefit management companies, health maintenance organizations or other institutions or health care organizations); and (f) payments or rebates paid in connection with sales to any governmental authority in respect of any state or federal Medicare, Medicaid or similar programs. All calculations shall be made in accordance with GAAP.

1.33 **"Optimization"** means certain technical revisions of the Present Device.

1.34 **"Optimization Project"** means the project currently being performed according to the Feasibility Statement of Work No. 3, a copy of which is attached to Exhibit 2.2.

1.35 " **PARI Intellectual Property** " means all Intellectual Property owned or Controlled by PARI and its Affiliates, as of the Effective Date or during the term of this Agreement, including that which (a) relates to its formulation technology, including PARI's liposomal technology (but excluding with respect to Arikace), the Device or the manufacture or use of the Device, or (b) are necessary or useful for either Party to perform the Project, or (c) are necessary or useful for Transave, its Affiliates or Sublicensees to commercialize the Device with the Drug Product in the Transave Field. For clarity, PARI Intellectual Property includes without limitation all Existing PARI Data, existing PARI Know-how, Project Intellectual Property, all Patent Rights listed on Exhibit 1.35 and all Improvements (subject to Section 2.5.2).

1.36 " **Phase II Trial** " means a clinical trial of a drug product in human patients, the primary endpoints of which are to define the optimal dose and clinical end points that will be used during a Phase III Trial.

1.37 " **Phase III Trial** " means a clinical trial of a drug product conducted in an expanded patient population at multiple sites, which is statistically powered and designed to definitively establish safety and efficacy with respect to a particular indication of one or more particular doses in the patients being studied and to provide the statistical and clinical basis for Regulatory Approval of such drug product.

1.38 **"Present Device"** means the present configuration no. 40L of eFlow, having the performance characteristics ascribed to such configuration in Exhibit 1.38.

1.39 " **Products** " means the individual Drug Product and/or the Device for use with the Drug Product.

1.40 " **Project** " means all activities to be performed by PARI, individually or jointly with Transave or third parties, that are set forth in a specific Work Plan.

1.41 " **Project Director** " means a development executive appointed by each Party to serve as such Party's principal coordinator and liaison for the Project. Except in the case of an emergency, each Party agrees to provide thirty (30) days written notice to the other Party prior to replacing its Project Director. The initial Project Directors shall be: [***] for PARI and [***] for Transave.

1.42 " **Project Intellectual Property** " means all Intellectual Property that is invented or created in the course of performance of a Work Plan under this Agreement, including without limitation any Intellectual Property directed to the Nebulizer apparatus, components or methods of manufacture thereof, regardless of who develops it. For clarity, the Project Intellectual Property excludes the Project Data, the Existing PARI Data, Existing Transave Data, and any Know-how owned or Controlled by PARI or Transave prior to the Effective Date and any Intellectual Property solely relating to Arikace.

1.43 " **Project Rate** " with respect to activities under a Work Plan means [***].

1.44 **"Qualified Stock"** means the series of preferred stock issued by Transave in the Most Recent Qualified Financing. As of the date of this Agreement, the Qualified Stock is Transave's Series D Convertible Preferred Stock.

1.45 **"Qualified Stock Price"** means the price per share paid by the purchasers of Qualified Stock in the Most Recent Qualified Financing (as equitably adjusted for any stock dividend, stock split, combination, reorganization, recapitalization, reclassification or similar event with respect to such Qualified Stock). As of the date of this Agreement, the Qualified Stock Price is $0.2001 per share.

1.46 **"Recall"** means a recall, withdrawal, or field correction of any product for any reason, or a dissemination of information regarding such product due to a change in the labeling of such product.

1.47 " **Regulatory Authority** " means any national (e.g., the FDA), supra-national (e.g., the European Commission, the Council of the European Union, or the EMEA), or other governmental entity in the Territory involved in regulation of or the granting of Marketing Approval for the Products or the development, manufacture, use or commercialization thereof.

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 continuing until the later of (a) Expiration of the last Valid Claim covering the particular Device in the particular country in which such Product is sold or (b) [***] after First Commercial Sale of the Drug Product in such country in the Transave Territory.

1.49 " **Sale of Business Transaction** " means the sale or transfer by Transave, directly or indirectly, of all of its rights in the Drug Product to a third party, excluding Affiliates of Transave, during the term of this Agreement. A change of "control" in Transave shall be deemed a Sale of Business Transaction. For the purpose of this definition, an individual corporation or other entity shall be deemed to "control" another corporation if it owns, directly or indirectly, more than fifty percent (50%) of the voting shares, or has the power to elect more than half the directors, of such corporation.

1.50 " **Secondary Indication(s)** " means the pulmonary administration of Drug Product for the treatment or prophylaxis of one or more of the following: [***] or [***], provided, however, that [***], and the treatment of such indications with [***], [***] and/or the [***] devices shall be excluded from the definition of Secondary Indications.

1.51 " **Specifications** " means the specifications, performance characteristics, parameters and requirements for the Device or other deliverables set forth in a Work Plan or user requirement specifications agreed to in writing between the Parties. The initial Specifications for the Present Device and the currently anticipated target Device are set forth in Exhibit 1.38. Transave shall amend Exhibit 1.38 to (i) amend existing parameters or add additional parameters to, the original Specifications for the Device as necessary or desirable based on results of the clinical data, or (ii) add an additional set of Specifications for a Device for a Secondary Indication. Amendments shall be made by Transave and submitted in writing to PARI for approval, which shall not be unreasonably withheld. After approval by PARI, each amendment shall become part of this Agreement and incorporated herein. Each amendment shall be substantially in the format of Exhibit 1.38 and sequentially labeled (Exhibit 1.38A, Exhibit 1.38B, etc.), and shall indicate if it supersedes any of the previous Exhibits 1.38.

1.52 " **Sublicensee** " means any person or entity who receives a sublicense from Transave under Section 4.1 of this Agreement to Exploit the Device with the Drug Product to a non-Affiliate Third Party.

1.53 " **Third Party License Agreement** " [***].

1.54 " **Transave Field** " means the pulmonary administration of Drug Product for the treatment or prophylaxis of cystic fibrosis (CF) and/or bronchiectasis. In addition, upon request or election by Transave, the "Transave Field" shall further include one or more of the Secondary Indications, subject to and in accordance with the provisions of Section 2.6.

1.55 " **Transave Intellectual Property** " means all Intellectual Property owned or Controlled by Transave and its Affiliates, as of the Effective Date or during the term of this Agreement, including that which (a) relates to its liposomal formulation technology, (b) is reasonably necessary or useful for either Party to perform the Project but excluding all Improvements, or (c) that solely relates to the Drug Product and is invented or created in the course of performance of a Work Plan or under this Agreement. For clarity, Transave Intellectual Property includes without limitation all Existing Transave Data, existing Transave Know-How and the Project Data (subject to the restrictions set forth in Section 3.2 (b)).

1.56 " **Transave Territory** " means the entire world.

1.57 " **Valid Claim** " means a claim in an issued patent within the PARI Intellectual Property, including the Project Intellectual Property, which has not Expired.

1.58 " **Work Plan** " means the activities, deliverables, timelines, Specifications and budget for the Project, established by the Parties pursuant to Section 2.2.

Article 2 – Development Project

2.1 **Scope of the Project** . Subject to the terms and conditions of this Agreement, the Parties shall collaborate, in accordance with one or more Work Plan(s), for Optimization of the Device for use with the Drug Product.

2.2 **Work Plans.** The initial Work Plan is set forth in Exhibit 2.2, which may be amended by Transave based on the results of the Optimization Project with the consent of PARI, such consent not to be unreasonably withheld. Additional Work Plans may be added, sequentially numbered as Exhibit 2.2A, 2.2B, etc., and attached to this Agreement. Transave may request additional services to be performed by PARI or request changes to any existing Work Plan(s), all in accordance with this Section 2.2.

(a) Upon any such request by Transave which shall specify deliverables and Specifications **,** PARI shall promptly prepare and submit to Transave a draft Work Plan or an amendment based on such request, setting forth in reasonable detail the services to be performed, the time and FTEs required for such services, timelines for the performance and completion of such services, and a budget for any out-of-pocket costs required to be expended. It is understood that PARI may also propose additional Work Plans or amendments on its initiative, and shall submit a draft thereof to Transave in the same form for approval by Transave.

(b) The Parties shall negotiate in good faith the final version of any additional Work Plan or amendment to a Work Plan, any of which shall be effective only after mutual agreement by the Parties thereon in writing. In the event of any conflict between a Work Plan and the terms and conditions of this Agreement, this Agreement shall control.

(c) PARI shall use Arikace or Drug Product provided to PARI solely for the purpose of Optimization of the Device pursuant to a Work Plan and shall not use Arikace or Drug Product for any other purpose. PARI shall not formulate, modify or reverse engineer the Drug Product or Arikace.

(d) Transave and its permitted Sublicensees shall use the Device solely with the Drug Product in accordance with the terms of this Agreement and shall not modify or reverse engineer the Device.

2.3 **Management** .

2.3.1 **Joint Steering Committee** . Promptly after the Effective Date, Transave and PARI shall establish a joint steering committee (the " **Joint Steering Committee** " or " **JSC** "), comprising three members chosen by each Party, to oversee, review and coordinate the activities of the Parties under this Agreement, including the performance of the Project and the development, manufacture and commercialization of the Product. The JSC shall be responsible for: (a) overseeing the activities of the Parties under this Agreement; (b) resolving disputes and disagreements under this Agreement; and (c) undertaking or approving such other matters as are specifically provided for the JSC under this Agreement. JSC will be responsible for developing a full charter for the Joint Steering Committee, and obtain written approvals from the CEO (as defined below) of the Parties. JSC meetings that must take place in person shall alternate between the place of business of each Party, unless otherwise agreed to by the Parties. Written minutes of all meetings will be provided within ten (10) business days of the meeting/teleconference to the members of the JSC.

2.3.2 **Decision Making.** Decisions of the Joint Steering Committee shall be made by unanimous vote of the members present in person or by other means (e.g., teleconference) at any meeting, with at least one representative from each Party participating in such vote. In the event that the JSC is unable to reach unanimity with respect to a particular matter, then either Party may, by written notice to the other, have such matter referred to the President or Chief Executive Officer (" **CEO** ") of each of the Parties, who shall discuss and attempt to resolve such matters to the Parties' mutual satisfaction within thirty (30) days thereafter. If the Parties are unable to resolve such dispute in accordance with this Section 2.3.2, Article 14 of this Agreement shall apply.

2.3.3 **Reserved Rights.** Notwithstanding the foregoing, however, in the event either Party reasonably determines that a final decision of the JSC pursuant to Section 2.3 will result in a hazardous or unsafe Device or Drug Product, or infringement of a third party's patent rights, then that first Party shall provide the JSC with information supporting its belief. Upon delivery of such information, and discussion with the second Party at the JSC, the first Party shall have the right to refrain from implementing such decision in its performance of this Agreement, provided that if the second Party in good faith disagrees with the basis of such determination, the Parties shall resolve the disagreement in accordance with Section 2.3.2. Notwithstanding the foregoing, nothing in this Article 2 shall be deemed to require either Party to take any action that it believes is unlawful.

2.3.4 **Limited Authority** . The decisions of the JSC, whether under this Section 2.3 or under any other section of this Agreement, shall not have the power to amend or contradict the terms of this Agreement or the agreed upon Work Plans, nor substitute for either Party's ability to exercise any right, nor excuse the performance of any obligation, set forth in this Agreement.

2.4 **Conduct of the Project** . Subject to the terms and conditions of this Agreement, each Party shall use Commercially Reasonable Efforts to perform the activities assigned to it under a Work Plan in accordance with the Specifications, timelines and budgets set forth therein, under the supervision of the JSC. Each Party shall keep the JSC informed as to its progress under a Work Plan.

2.5 **Improvements.** Notwithstanding anything to the contrary in this Agreement, if PARI develops an incremental Improvement, then PARI shall incorporate such Improvement into the Device, without further consideration, if (i) it is not contractually prohibited from doing so by the agreement under which such Improvement was developed, (ii) PARI generally incorporates such Improvement into an eFlow for use in CF, Bronchiectasis or such Secondary Indication (but in this instance only, without reference to the Drug Product contained in the definition of Secondary Indication in Section 1.50) that has been included in the Transave Field pursuant to Section 2.6, and (iii) it is consistent with the Specifications and the applicable regulatory requirements. If an Improvement is not an incremental Improvement (e.g., a major Improvement or a new 510(k) is or will be filed), then PARI shall, to the extent it has the right to do so, offer Transave an opportunity to review such Improvement for a period of sixty (60) days from receipt of a description of such Improvement and a plan for development of such Improvement and possible incorporation into the Device in order for Transave to determine whether it wishes to have such Improvement incorporated into the Device and thereby be incorporated into the license granted pursuant to Section 4.1. If Transave determines (by giving written notice to PARI) within such sixty (60) day period that it desires to benefit from the Improvement and include the Improvement in the Device, such Improvement shall be automatically included in PARI Intellectual Property. If Transave does not give written notice to PARI within the sixty (60) day period of its desire to benefit from the Improvement, Transave shall be deemed to have rejected the Improvement and PARI shall have no obligation to include the Improvement in the Device. Notwithstanding anything to the contrary in this Agreement, if PARI develops an Improvement and desires to obtain patent protection for such Improvement, PARI shall be free to obtain such protection and may take all steps necessary, appropriate or advisable thereto, provided that Transave's rights under this Agreement shall not be restricted or limited in any way.

2.6 **Designation of Secondary Indication.** During the Term, if Transave desires to add one or more Secondary Indications to the Transave Field it will notify PARI thereof in writing. Also, if at any time during the Term of this Agreement, PARI negotiates with a third party to license PARI Intellectual Property in one or more Secondary Indications, PARI agrees that, prior to entering into a binding definitive licensing agreement, whether oral or written, whether in the form of an agreement, term sheet, letter of intent or other format, with such third party, PARI shall provide notice to Transave of such negotiations and shall offer to Transave the option to add such Secondary Indication(s) to the Transave Field; provided, however, that PARI shall not be obligated to offer such Secondary Indication to Transave if Transave has already entered into a binding definitive licensing agreement, whether oral or written, whether in the form of an agreement, term sheet, letter of intent or other format, for another Nebulizer with a third party for such Secondary Indication. Transave shall have thirty (30) days from the date of receipt of notice to exercise this option by sending a written notice thereof to PARI.

Notwithstanding the foregoing, PARI shall be permitted to conduct development activities on its own or with a third party with respect to the Secondary Indications, including feasibility studies and the notice obligation and right of first refusal of Transave shall not apply thereto. If Transave desires to add a Secondary Indication either pursuant to the first sentence of this paragraph or by exercising its option, the Parties shall negotiate in good faith commercially reasonable and mutually acceptable diligence requirements, non-compete provisions, termination rights and such other terms and conditions as the Parties may identify for the applicable Secondary Indication(s), [***]

2.7 [***]. At any time, the Parties may agree to discuss a potential license agreement related to [***] for use with Arikace.

2.8 **Project Fees** . Transave shall compensate PARI for its performance of the Work Plans at the Project Rate [***] (" **Project Fees** "). The Project Fees shall be invoiced to and paid by Transave in accordance with Section 9.1 below. Except for the compensation and reimbursement set forth in this Section 2.8, each Party shall perform all of its activities under the Work Plans at its own cost.

2.9 **Reports.** PARI's obligations to provide reports will be as specified in individual Work Plans. In addition to any meetings, working groups or reviews required under the Work Plan, PARI shall provide Transave with reasonable access to the Project Director, from time to time throughout the term of the applicable Work Plan. Such access shall be at Transave's reasonable request, during regular business hours and mutually convenient times, and may include (without limitation) teleconferences, email, face-to-face meetings or other visits to PARI's facility.

2.10 **Subcontractors** . PARI shall not subcontract its performance of the Project to another entity without Transave's prior written approval, which approval shall not be unreasonably withheld, delayed or conditioned. In any case, PARI shall remain completely responsible for all acts and omissions of its subcontractors for any Project activities that are subcontracted.

Article 3 – Intellectual Property

3.1 **Existing Intellectual Property Ownership and Limited License Grant** .

(a) Transave shall exclusively own the Transave Intellectual Property and any improvements, enhancements or modifications in and to the foregoing conceived or developed by either Party pursuant to this Agreement. Except for the license expressly granted in 3.1(b), no other license in the Transave Intellectual Property is granted to PARI by implication, estoppel or otherwise. PARI shall exclusively own the PARI Intellectual Property and any improvements, enhancements or modifications in and to any of the foregoing conceived or developed by either Party pursuant to this Agreement, including all Improvements. Except for the licenses expressly granted in this Agreement, no other license in the PARI Intellectual Property is granted to TRANSAVE by implication, estoppel or otherwise.

(b) Subject to the terms and conditions of this Agreement, Transave hereby grants PARI a royalty-free, non-exclusive, non-transferable (except to its Affiliates and as expressly provided herein) license under the Transave Intellectual Property solely to perform PARI's obligations and responsibilities under the Work Plans and this Agreement. PARI hereby grants to Transave, until initiation of the Royalty Term, a royalty-free, non-exclusive license under the PARI Intellectual Property and PARI Project Intellectual Property solely to perform Transave's activities, under this Agreement including the development of Drug Products, provided, however that all Improvements shall be exclusively owned by PARI and Transave shall not file any patent application that incorporates the PARI Intellectual Property and/or the Project Intellectual Property.

3.2 **Project Intellectual Property Ownership and Project Data Ownership** .

(a) PARI shall exclusively own the Project Intellectual Property. Transave agrees to assign and hereby assigns to PARI all right, title and interest in and to Project Intellectual Property.

(b) Subject to Section 3.3 below, Transave shall exclusively own all Project Data; provided, however, that Transave (i) shall not use any Project Data with, or share, transfer or license to PARI Competitor pursuant to Section 4.1.3 below and (ii) Transave shall not file any patent application or amendment that incorporates the PARI Intellectual Property and/or the Project Intellectual Property in the claims thereof. Transave shall give PARI reasonably sufficient advance notice and opportunity to review any patent applications, prior to filing, that first incorporate any particular PARI Intellectual Property or Project Intellectual Property. If, within fifteen (15) days after receipt, PARI notifies TRANSAVE in writing that TRANSAVE's patent application contains PARI Intellectual Property or Project Intellectual Property that is patentable but for which PARI has not previously filed for patent protection, then TRANSAVE agrees to delay filing of its application for an additional thirty (30) days, to permit PARI to prepare and file a patent application to protect such PARI Intellectual Property or Project Intellectual Property. In the event Transave nevertheless files a patent application that claims the PARI Intellectual Property or any Project Intellectual Property, then PARI shall receive a non-exclusive, perpetual, world-wide, fully paid-up, sublicensable, unrestricted, irrevocable right and license to research, formulate, develop, seek regulatory approval for, make, have made, use, sell, have sold, offer for sale, market, promote, import, export, display, make derivative works of, copy, distribute, perform, license, sublicense or otherwise commercialize, exploit or dispose of the PARI Intellectual Property or any Project Intellectual Property to the extent claimed in such patent application and/or patent. In the event that Transave uses Project Data (that have been generated based on the utilization of the Device) to file a patent application, then PARI shall have a non-exclusive, perpetual, world-wide, fully paid-up, licensable, unrestricted right and license (outside of the Transave Field) (1) to practice under any apparatus claim that claims a Device, Nebulizer that is proprietary to PARI, or component thereof, and any method of manufacture claim that claims a method of manufacturing a Device, Nebulizer that is proprietary to PARI, or component thereof, in any such patent that is based on such Project Data , and (2) to practice under any method of use claim that is a method of using a Device, Nebulizer that is proprietary to PARI, or component thereof, in any such patent that is based on such Project Data to the extent necessary to avoid any liability on PARI's part for infringement of such method of use claims. Notwithstanding anything to the contrary in the foregoing, PARI shall not obtain any rights under this Section 3.2(b) to Exploit any Transave proprietary drug product or formulation thereof.

3.3 **Default on Project Fees** . Subject to Article 14, in the event of a default in the payment of any undisputed Project Fees under this Agreement, which default is not cured within thirty (30) days after Transave receives written notice thereof by PARI referencing this Section 3.3, specifying in detail the amount of Project Fees alleged to be unpaid and a calculation thereof, and providing all relevant supporting documentation evidencing such calculation, then Transave shall not have the right to use such specific Project Intellectual Property and Project Data that was conceived or developed by PARI that was not paid for in accordance with the Work Plan by Transave. In such event, however, it is understood that Transave shall retain the right to use and Exploit other Project Intellectual Property and Project Data that Transave has fully paid for in accordance with the Work Plan and this Article 3.

3.4 **Scientific Records** . PARI shall maintain laboratory notebooks and all technical, scientific, accounting and other records in sufficient detail and which shall reflect work done, results achieved, intellectual property developed, including all data in the form required by Applicable Laws and Standards, which shall be kept for three (3) years after completion or termination of the respective Work Plan or any longer period mandated by Applicable Laws and Standards. However, records supporting the relevant PARI Patent Rights and the Project Intellectual Property shall be kept for the longer of a period of fifteen (15) years after First Commercial Sale of Drug Product in any country in the Transave Territory or 20 years from the date of filing of any intellectual property related to this project or a longer period mandated by Applicable Laws and Standards.

3.5 **Patent Protection** . Except as set forth in Section 3.6 with respect to the Joint Patents, PARI has the sole discretion and responsibility, at its expense, to prepare, file, prosecute, maintain, defend, and enforce any patent applications and patents, as applicable, to PARI Intellectual Property and Project Intellectual Property. TRANSAVE has the sole discretion and responsibility at its expense, to prepare, file, prosecute, maintain, defend, and enforce any patent applications and patents, as applicable, to TRANSAVE Intellectual Property. In any case and pursuant to this Section 3.5, TRANSAVE shall not, without PARI's prior written consent, to be withheld in its sole discretion, prepare, file, prosecute, maintain, defend, or enforce any patent applications and patents, as applicable, relating to the Device or any other eFlow or otherwise incorporate PARI Intellectual Property and/or the Project Intellectual Property, including but not limited to eFlow, or PARI's proprietary TouchSpray ® Technology. In any case and pursuant to this Section 3.5, PARI shall not, without Transave's prior written consent, to be withheld in its sole discretion, prepare, file, prosecute, maintain, defend, or enforce any patent applications and patents, as applicable, relating to the Drug Product.

3.6 **Joint Patents.** PARI and Transave are currently discussing the potential of filing a joint patent application (the **"Joint Patent"**). The Parties hereby agree that no Joint Patent application shall be filed without (i) the consent of the other Party and (ii) the Parties having entered into an Addendum to this Agreement outlining the respective rights and obligations, including provisions regarding ownership, rights of use, restrictions of use, prosecution, enforcement and defense, with respect to the Joint Patent.

Article 4 – Commercial License

4.1 Commercial License

4.1.1 **Exclusive Grant in Transave Field** . During the Royalty Term, PARI hereby grants Transave a royalty-bearing exclusive right and license in the Transave Territory, (with the right to grant and authorize sublicenses, except with respect to [***] which PARI shall sublicense at Transave's request according to Section 4.1.4, provided (x) such Sublicensees agree to be bound by the terms of this Agreement, (y) Transave shall nonetheless remain liable to PARI for any breach by a Sublicensee of this Agreement and (z) such Sublicensee is not a PARI Competitor pursuant to Section 4.1.3 below), under PARI Intellectual Property and Project Intellectual Property to Exploit (subject to Section 4.1.1 below) the Device for use with the Drug Product in the Transave Field; provided, however, that Improvements are governed by Section 2.5.2. For clarity, the license of this Section 4.1.1 shall be exclusive, except with respect to the [***], in the Transave Field even as to PARI, and PARI shall not practice itself, nor grant to a third party, any rights with respect to PARI Intellectual Property or Project Intellectual Property for use in the Transave Field in the Transave Territory, except with respect to the [***]. Upon expiration of the Royalty Term, the foregoing license shall be rendered non-exclusive, fully paid-up and royalty-free, on a country-by-country basis; provided, however, that upon Transave's written request, such license shall remain exclusive, on a country-by-country basis, subject to Transave's continued payment of royalties for such country as set forth in Section 6.1 of this Agreement.

4.1.2 **Manufacturing Rights** . Transave covenants that it shall not, and it shall cause its Affiliates and permitted Sublicensees not to, exercise rights to manufacture the Device for use with the Drug Product, the Device, the Device Accessories or any components of any of the foregoing under the license of this Section 4.1 except pursuant to a fully executed Commercial Supply Agreement as set forth in Section 8.9 of this Agreement.

4.1.3 **Restriction of Certain Sublicenses** . Transave shall not grant to a PARI Competitor a sublicense under the PARI Intellectual Property without PARI's prior written consent. For such purposes a " **PARI Competitor** " shall mean an entity identified in Exhibit 4.1 hereto.

4.1.4 **Sublicense of** [***]. Transave acknowledges that a portion of the PARI Intellectual Property includes PARI's rights under the Third Party License Agreement. In the event Transave transfers or sublicenses the license granted in this Section to a third party, such rights shall be excluded from such transfer or sub-license. However, in the event that Transave transfers or sublicenses to a third party any of the license rights granted in this Section 4.1, upon Transave's request, PARI shall directly grant to such third party a sublicense of PARI's rights under the Third Party License Agreement for no additional consideration, other than that already due to PARI under this Agreement with respect to any transfer or sublicense of rights granted to Transave in this Section 4.1. Such transfer or sublicense shall be subject to the terms and conditions of this Agreement.

4.2 **Exclusivity of Efforts** . The Parties acknowledge and agree that nothing contained in this Section 4.2 shall limit PARI from researching, developing, manufacturing, or commercializing medical devices (including existing devices) as stand alone devices outside of the Transave Field other than the Device (subject to PARI's obligations under Section 2.6).

(a) **Non-Compete** . 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 not compete with Transave (x) in CF and/or Bronchiectasis with a Competing Nebulizer in the Transave Field, within the Transave Territory, or (y) otherwise engage in the research, development, manufacture and/or commercialization of amikacin for pulmonary administration using a Competing Nebulizer. In addition, during the term of this Agreement, PARI agrees that it and its Affiliates shall not compete with Transave or otherwise engage in the research, development, manufacture and/or commercialization of any liposomal formulation of 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 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 for any indication (including clinical development and clinical research), including CF and Bronchiectasis, and that such uses shall not conflict with the prohibitions of this Section 4.2(a).

(b) **Transave Diligence** . PARI's obligations under Section 4.2(a) shall be conditioned upon Transave complying with its diligence obligations as set forth in Sections 7.1 and 7.2.

(c) During the term of this Agreement, Transave agrees that it and its Affiliates shall not compete with PARI or otherwise engage in the research, development manufacture and/or commercialization of any liposomal formulation of cyclosporin.

4.3 **Rights in Bankruptcy** . All rights and licenses granted under or pursuant to any section of this Agreement are, and shall be deemed to be, for purposes of Section 365(n) of the Bankruptcy Code, 11 U.S.C. § 101 et seq., licenses of rights to "intellectual property" as defined under Section 101(35A) of the Bankruptcy Code. The parties shall retain and may fully exercise all of their respective rights and elections under the Bankruptcy Code.

Article 5 – Upfront License Fee and Milestones

5.1 **Upfront License Fee.** After execution of this Agreement and within thirty (30) days after receipt of written notice of PARI's election under Section 5.3(a), Transave shall pay PARI (a) [***] either in cash, or the equivalent in Qualified Stock, or a

combination of cash and Qualified Stock, at PARI's option as provided in section 5.3(a) below, plus (b) the equivalent of [***] in Qualified Stock, as an upfront license fee.

5.2 **Milestones.** In further consideration of the rights and license granted by PARI under this Agreement, Transave agrees to make the following milestone payments to PARI, upon the first achievement of the corresponding events set forth below by or under authority of Transave, within thirty (30) days after Transave's receipt of written notice of PARI's election under Section 5.3(b) below. For avoidance of doubt, each Milestone Payment is payable only once.

MILESTONE EVENT	MILESTONE PAYMENT
1. Receipt of any positive trial report from the first Phase IIb Trial that are sufficient to support the advancement of Drug Product development with the Device into the first Phase III Trial	[***] either in cash, Qualified Stock or a combination of cash and Qualified Stock; plus [***] in Qualified Stock
2. Initiation of the first Phase III Trial of Drug Product with the Device	[***] either in cash, Qualified Stock or a combination of cash and Qualified Stock
3. First Acceptance of MAA (or equivalent) submission in the US for such Drug Product with the Device	[***] either in cash, Qualified Stock or a combination of cash and Qualified Stock
4. First receipt of Marketing Approvals in the United States for both (i) such Drug Product and (ii) the Device	[***] either in cash, Qualified Stock or a combination of cash and Qualified Stock
5. First receipt of Marketing Approvals in the first of the Major EU Countries for both (i) such Drug Product and (ii) the Device, in the same Major EU Country	[***] either in cash, Qualified Stock or a combination of cash and Qualified Stock
Total	[***]

5.3 **Equity Issuances.** Subject to the limitations set forth in Sections 5.3(d) and 5.3(e) below, PARI may elect, as set forth below, to receive any or all of the payments set forth in Sections 5.1 and 5.2 above in the form of Qualified Stock in lieu of cash, as set forth below in this Section 5.3.

(a) **Upfront License Fee.** Within thirty (30) days of the execution of this Agreement and provided PARI has received the information set forth in paragraphs (b)(iii) and (iv) below, PARI shall notify Transave in writing whether or not it elects to receive Qualified Stock in lieu of the upfront license fee payment of [***] set forth in Section 5.1(a) above. If PARI fails to make its election within such thirty (30) days and provided PARI has received the information set forth in paragraphs (b)(iii) and (iv) below, then Transave may, in its sole discretion, make such payment in cash, Qualified Stock or a combination of cash and Qualified Stock, in the manner set forth in Section 5.3 (c) below.

(b) **Milestone Payments.** Promptly following the occurrence of each of the Milestone Events specified in Section 5.2 above, Transave shall provide to PARI (i) written notification that such milestone event has occurred; (ii) to the extent not previously provided, a summary of the terms of the Qualified Stock that PARI may elect to receive in connection therewith; (iii) to the extent not previously provided, copies of any voting agreement or co-sale agreement to which other holders of such Qualified Stock are parties, as well as any other document restricting the transferability of such shares of Qualified Stock; and (iv) such financial or other information reasonably requested by PARI. For the avoidance of doubt, all materials and other information provided to PARI pursuant to this Section 5.3 shall be deemed to be Confidential Information subject to Article 11 of this Agreement. PARI shall, within thirty (30) days after Transave's delivery of the foregoing information, notify Transave in writing whether or not it elects to receive Qualified Stock in lieu of the cash milestone payment applicable to such milestone event. If PARI fails to make its election within such thirty (30) days, then Transave may, in its sole discretion, make such payment in cash or Qualified Stock, in the manner set forth in Section 5.3(c) below.

(c) **Calculation of Number of Shares of Qualified Stock.** [***]

(d) **Conditions to Issuance of Equity** . In the event that Transave issues Qualified Stock to PARI hereunder, the share certificate(s) evidencing such Qualified Stock shall be endorsed with customary securities legends, and the issuance of such Qualified Stock shall be subject to applicable federal and state securities laws and the restrictions and other terms of Transave's bylaws and other organizational documents. In addition, PARI must as a condition precedent to the receipt of such Qualified Stock: (i) if requested by Transave, agree to become bound by any voting agreement, co-sale agreement or other transfer restrictions applicable to the other holders of such Qualified Stock and (ii) make such additional representations and warranties at the time of the issuance of such Qualified Stock as may be reasonably requested by Transave to ensure compliance with applicable federal and state securities laws. In the event Transave has completed an initial public offering of its capital stock prior to the occurrence of a Milestone Event for which PARI would be entitled to elect to receive Qualified Stock in lieu of a cash milestone payment, or Transave otherwise reasonably concludes that it is unable to comply with applicable federal and state securities laws in connection with any particular issuance of Qualified Stock to PARI pursuant to this Section 5.3, Transave shall have no obligation to issue such Qualified Stock, but if such Qualified Stock is not issued, Transave shall pay PARI the amount of [***] (for the upfront license fee set forth in Section 5.1), [***] (for Milestone Event 1 set forth in Section 5.2), [***] (for Milestone Events 2 and 5 set forth in Section 5.2), [***] (for Milestone Event 3 set forth in Section 5.2) or [***] (for Milestone Event 4 set forth in Section 5.2), as applicable, upon the occurrence of the obligation to pay the upfront license fee or milestone payment specified in Section 5.1or in Subsections 1 through 5 of Section 5.2 above, as applicable, within thirty (30) days of Transave reasonably concluding that it is unable to issue such Qualified Stock. For the avoidance of doubt, Transave's obligation to issue Qualified Stock under this Section 5.3 shall not apply to an initial public offering of Transave's capital stock, and shall only apply with respect to the Qualified Stock issued in the Most Recent Qualified Financing but not to any warrants, promissory notes or other securities which may be issued concurrently to the investors in such Most Recent Qualified Financing.

(e) **Effect of Sale of Business Transaction** . In connection with any Sale of Business Transaction which closes prior to any particular issuance to PARI of Qualified Stock, the successor in interest to Transave shall have the option (but not the obligation) to assume Transave's obligation to issue Qualified Stock pursuant to this Section 5.3 by issuing capital stock of the successor in interest at the applicable conversion ratio for the Qualified Stock in such Sale of Business Transaction, subject to PARI having (x) received documents and information with respect to the capital stock of such successor in interest substantially similar to the documents and information set forth in Sections 5.3(b)(ii), 5.3(b)(iii) and 5.3(b)(iv) above and (y) agreed in writing within thirty (30) days of receipt of all such documents and information that it elects to receive capital stock of the successor in interest as the method of payment. If such successor in interest does not elect to assume such obligation or PARI has not elected to receive capital stock of such successor in interest, then such successor in interest shall immediately pay PARI the amount of [***] (for the upfront license fee set forth in Section 5.1), [***] (for Milestone Event 1 set forth in Section 5.2), [***] (for Milestone Events 2 and 5 set forth in Section 5.2), [***] (for Milestone Event 3 set forth in Section 5.2) or [***] (for Milestone Event 4 set forth in Section 5.2), as applicable, upon the occurrence of the obligation to pay the upfront license fee or milestone payment specified in Section 5.1 or in Subsections 1 through 5 of Section 5.2 above, as applicable, and PARI shall have no right to capital stock or equity of Transave or such successor in interest thereafter.

Article 6 – Royalties

6.1 **Royalties for Drug Products** . In further consideration of the rights and license granted by PARI under this Agreement, during the Royalty Term, subject to the terms and conditions of this Agreement, Transave agrees to pay PARI a royalty equal to [***] of the Net Sales of Drug

Product sold by Transave, its Affiliates or Sublicensees. Such royalties shall be paid in accordance with Section 9.2 below.

6.2 **Combination Products** . In the event (i) a Drug Product is sold in combination with the Device or other components for a single price, or (ii) a Drug Product is sold in combination with services or other products, amounts invoiced for such combination sales for purposes of calculating Net Sales of the Drug Product in such combination shall be reasonably allocated between such amounts attributable to the Drug Product and amounts attributable to the Device, other components, services or other products (" **Non-Royalty Components** "), by or under authority of Transave. Such allocation shall be based on the relative value(s) of the Drug Product and of the Non-Royalty Components, and if the Parties are unable to agree on such allocation, the allocation shall be determined in accordance with Article 14.

6.3 **Annual Minimum Royalties** . During the Royalty Term, Transave shall pay to PARI an Annual Minimum Royalty in US dollars in accordance with Section 9.3 below; provided, however, that, in the event Transave has permanently discontinued to Exploit the Drug Product for CF in accordance with Section 7.1(a), then the Annual Minimum Royalty shall no longer be applicable for the Drug Product for CF but the obligation to pay Annual Minimum Royalties for the Drug Product for Bronchiectasis shall remain in effect.

(a) **Determining the Annual Minimum Royalty.**

(i) The " **Annual Minimum Royalty** " shall be determined by the following table.

Year of Sales	Annual Minimum Royalty
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]
[***]	[***]

(b) **Failure to pay Annual Minimum Royalty.** In the event Transave does not pay the Minimum Royalty Payment due under Section 6.3(a) above when due, PARI shall have the right to (i) render non-exclusive the license set forth in Section 4.1.1 upon written notice to Transave and failure to cure within sixty (60) days, and the non-compete obligations set forth in Section 4.2(a) shall immediately cease and (ii) terminate immediately the license set forth in section 4.1.1 for CF or Bronchiectasis, as applicable, if the Minimum Royalty Payment (plus all interest due pursuant to Section 9.5) plus an amount equal to [***] of the then applicable Minimum Royalty Payment has not been paid within six (6) months of the initial due date of the Minimum Royalty Payment; provided, however, that if all such payments have been made by Transave to PARI within such six (6) months period, then the license shall become exclusive again and the non-compete obligations set forth in Section 4.2 (a) shall be reinstated immediately, as of the date of payment. The royalty rates set forth in this Article 6 shall remain unchanged due to the license of Section 4.1.1 becoming non-exclusive.

6.4 **Infringement or Misappropriation of Third Party Rights** . In the event of an actual or threatened infringement action pertaining to the Device, which causes, or could reasonably be expected to cause, Transave's use of the Device to be disrupted, PARI shall, at its option and on a country by country basis, (i) provide Transave with access to components or entire nebulizers which are functionally equivalent to the infringing elements of the Device while still meeting the Specifications, without additional charge (" **Option 1** "); (ii) modify the infringing portions of the Device to avoid the infringement while still meeting the Specifications (" **Option 2** "); or (iii) obtain a license for Transave to continue use of the Device for the Term of this Agreement, and pay for any additional fee required for a license with the Third Party Controlling the Intellectual Property which is infringed or misappropriated by the Device (" **Option 3** "). In the event PARI reasonably believes it to be Necessary (defined below) to proceed with obtaining a license for Transave as described above in Option 3, then PARI shall contribute up to a maximum amount of [***] in the aggregate of all Royalties paid by Transave to PARI pursuant to this Agreement towards the cost of such license. If at any time the anticipated costs for PARI to comply with Option 3 exceeds [***] in the aggregate of all Royalties paid by Transave to PARI pursuant to this Agreement, then PARI shall so notify Transave and Transave shall pay such additional amounts in order for PARI to secure such Necessary license. "Necessary" shall mean a determination by PARI after good faith consultation with Transave that a license would be prudent given the potential to resolve any claims or potential claims of Intellectual Property infringement or misappropriation.

Article 7 – Development, Regulatory and Commercialization Roles and Responsibilities

7.1 **Transave Development and Commercialization Diligence for CF** .

(a) Transave agrees to use Commercially Reasonable Efforts to pursue the clinical development of and to obtain Marketing Approval for CF for the Drug Product intended for use with the Device in one (1) or more countries (and at least in the United States), and after obtaining such Marketing Approval, to use Commercially Reasonable Efforts to market and sell the Drug Product with the Device in all countries in which it has been approved, except that Transave 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 Transave shall immediately notify PARI in writing of such decision and in such case CF shall no longer be included in the Transave Field and PARI's obligations under Section 4.2(a) shall no longer apply as to CF. Until such first Marketing Approval, provided that the license of Section 4.1.1 remains exclusive hereunder, Transave shall provide PARI, at least semi-annually through the JSC, with detailed reports of the progress of its development of Drug Products for use with the Device and plans for its development and commercialization thereof in the upcoming year. The JSC shall discuss such reports and plans and Transave shall duly consider any comments thereon provided by PARI, provided that the Parties agree that Transave shall retain sole control of its development efforts hereunder and its plans therefor. For clarity, it is understood that the obligation to use Commercially Reasonable Efforts as set forth in this Section 7.1 shall apply to any Affiliates and/or permitted Sublicensees who are responsible for development of Drug Products for use with the Device, and Transave shall share reports and plans from such Affiliates and/or permitted Sublicensees with PARI at least annually through the JSC in the same manner as for reports and plans of its own development. This Section 7.1 shall also apply to any permitted successors and assigns of Transave under this Agreement. Transave's breach of this Section 7.1(a) shall be deemed a material breach of this Agreement.

(b) The Parties agree that Transave will use Commercially Reasonable Efforts to meet the following milestones with respect to CF:

Milestone Activity	Milestone Deadline
1. **Diligence Milestone 1:** first Phase III Trial for CF begins	[***]
2. **Diligence Milestone 2:** first submission of an MAA application for CF in the Transave Territory	[***]

To the extent Transave does not meet a milestone listed above within the stated time period or the dates listed below, other than any failure resulting directly from a breach of this Agreement by PARI, then, subject to the provisions of Section 7.3, PARI shall have the option, in its sole discretion, to take the applicable action set forth below. Such option must be exercised by written notice to Transave (the "Diligence Termination Notice"), and shall become effective on the thirtieth (30 th) day following the date of the Diligence Termination Notice. PARI shall have the option to:

(i) with respect to Diligence Milestone 1 above, terminate its obligation not to compete with Transave in CF as set forth in Section 4.2 of this Agreement only. In the event Transave has still not achieved Diligence Milestone 1 by [***], then the license granted by PARI to Transave under this Agreement shall be rendered non-exclusive with regard to CF only. In the event Transave still has not achieved Diligence Milestone 1 by [***], then PARI shall have the option to terminate the licenses granted by PARI to Transave under this Agreement with regard to CF only by providing written notice to Transave thereof;

(ii) with respect to Diligence Milestone 2 above, terminate its obligation not to compete with Transave in CF as set forth in Section 4.2 of this Agreement only. In the event Transave has still not achieved Diligence Milestone 2 by [***], then the licenses granted by PARI to Transave hereunder shall be rendered non-exclusive with regard to CF only. In the event Transave still has not achieved Diligence Milestone 2 by [***], then PARI shall have the option to terminate the license granted by PARI to Transave under this Agreement with regard to CF only by providing written notice to Transave thereof;

7.2 **Transave Development and Commercialization Diligence for Bronchiectasis.**

(a) The Parties agree that Transave will use Commercially Reasonable Efforts to meet the following milestone with respect to Bronchiectasis:

Milestone Activity	**Milestone Deadline**
1. **Diligence Milestone 1:** Last patient to complete the Phase II Trial for Bronchiectasis	[***]
2. **Other Diligence Milestones:** see below	

Within one hundred eighty (180) days following the final results of the Phase II Trial for Bronchiectasis, the Parties, acting in good faith, will negotiate additional milestones that meet reasonable industry standards. If no additional milestones are agreed to within such time period, and the lack of milestones is not mutually agreed by both parties, then at PARI's option, PARI may by providing prompt written notice to Transave, (i) make the license granted to Transave under this Agreement non-exclusive and PARI's non-compete obligations set forth in Section 4.2 shall terminate or (ii) terminate the license granted to Transave under this Agreement, in each case solely with respect to Bronchiectasis.

If Transave fails to meet a milestone within the applicable time period, other than any failure resulting from a breach of this Agreement by PARI, then, subject to the provisions of Section 7.3, PARI shall have the option to render Transave's license hereunder non-exclusive solely with respect to Bronchiectasis and to terminate its obligation not to compete with Transave in Bronchiectasis as set forth in Section 4.2 of this Agreement. Such option must be exercised by sending the Diligence Termination Notice to Transave, and shall become effective on the thirtieth (30 th) day following the date of the Diligence Termination Notice. If such milestone is still not met within twelve (12) months of the applicable time period, other than any failure resulting from a breach of this Agreement by PARI, then, subject to the provisions of Section 7.3, PARI shall have the option to terminate the license granted to Transave under this Agreement with respect to Bronchiectasis only by providing written notice thereof to Transave.

(b) For the avoidance of doubt, subject to the provisions of Section 7.2(a), nothing in this Agreement shall impart any obligation on Transave to pursue the indication of Bronchiectasis, and Transave's activity or lack of activity with respect to Bronchiectasis shall not affect in any way Transave's rights in and to CF or any Secondary Indication.

7.3 **Updated Milestones.** In the event Transave is unable to achieve the milestones set forth in Sections 7.1(b) and/or 7.2(a), as applicable, because of a breach of PARI of this Agreement, or in the case the Phase II or the Phase III Trial has to be repeated or there are documented clinical holds or delays caused by requests of the Regulatory Authorities preventing Transave from proceeding, then the due dates set forth above for such Milestones shall be reasonably adjusted to account for such factors pursuant to mutual agreement of the Parties.

7.4 **Manufacture of Drug Product and Device** . As between the Parties, (i) Transave shall have the exclusive right to manufacture (or have manufactured) Drug Product for any and all purposes (including without limitation, for use with the Device, for clinical and for commercial use); and (ii) PARI shall have the exclusive right to manufacture Devices for use with the Drug Product, for clinical and for commercial use, except as otherwise may be provided in the Commercial Supply Agreement.

7.5 **Supply of Devices for Clinical Trials.** PARI shall supply Transave or its designee with all Devices, and Device Accessories, to the extent applicable, required for the conduct of clinical trials. Devices shall meet the Specifications. The manufacturing and supply of such Devices by PARI shall comply with Article 8 below.

(a) **Price** . The price charged by PARI for such Devices and related parts shall be equal to the prices set forth on Exhibit 7.5(a) for clinical supply of the Devices.

(b) **Initial Forecast** . An initial forecast of the Devices, including delivery dates, anticipated to be required by Transave for clinical trials is set forth in Exhibit 7.5(b). Such forecast shall not be binding on either Party, unless and until such quantities and dates are confirmed in written purchase orders issued by Transave and accepted by PARI or set forth in a Work Plan executed by the Parties. Transave agrees to provide PARI a lead time of at least two (2) months.

(c) **Accessories.** The provisions of this Section 7.5 apply equally to Device Accessories.

7.6 **Regulatory Matters.**

(a) **General** . As between the Parties, (i) Transave shall be responsible for, and shall control all filings and interactions with Regulatory Authorities with respect to the Drug Products, and Transave shall control all clinical and regulatory strategy for the Drug Products; and (ii) PARI shall be responsible for, and shall control all filings and interactions with Regulatory Authorities with respect to the Device, and PARI shall control all clinical and regulatory strategy for the Device. Any MAAs, Marketing Approvals, INDs, or other regulatory submissions, filings, approvals and documentation (collectively, " **Regulatory Filings** ") shall be submitted solely in the name of, and exclusively owned by, (x) Transave or its designee with respect to the Drug Product and (y) PARI or its designee with respect to the Device. Each Party agrees to cooperate with, and provide reasonable assistance to the other Party, in the preparation of such Regulatory Filings, at the other Party's expense.

(b) **Approvals for Device for Clinical Trials.** PARI represents, warrants and covenants that, with respect to the Present Device, it has been granted a 510(k) marketing clearance in the US and a CE mark in the European Union. Attached hereto as Exhibit 7.6(b) is a list of all countries in which PARI has obtained or is seeking Marketing Approval for the Present Device and PARI shall keep Transave informed of any change in status. Transave shall give reasonable weight to this list when choosing countries in which to conduct future clinical trials. If Transave chooses to conduct a clinical trial in a country in which the current status of approval is not adequate to allow Transave to conduct a clinical trial, then PARI hereby agrees to reasonably cooperate with Transave, at Transave's expense, in order to obtain the applicable regulatory approvals in such country to allow Transave to use the Device for clinical trials in such country.

(c) **Regulatory Inspections and Requests.** Transave and PARI shall cooperate in good faith with respect to the conduct of any inspections required by any Regulatory Authority of a Party's site and facilities related to Transave's clinical trials regarding Devices. Each Party shall promptly provide to the other Party a summary of any inspectional observations, inspection reports issued by a Regulatory Authority, or responses to a Regulatory Authority's inspectional observations or report related to such clinical trial. PARI agrees to promptly and timely respond to all requests from Regulatory Authorities and to promptly notify Transave about such requests.

7.7 **Adverse Event Reporting.** Unexpected serious adverse events that are made known to either party and that are considered to be related to the Drug Product or the Device, shall be reported to the other Party on an expedited basis, and at least within forty-eight (48) hours from the notification of an institutional review board (IRB), Regulatory Authority or participating investigators and in any case not longer than five (5) business days after the event was made known. An unexpected adverse experience is defined as any adverse drug experience, the specificity or severity of which is not consistent with the current Investigator Brochure for a clinical trial, or, if an Investigator Brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. Unexpected, as used in this definition, refers to an adverse drug experience that has not been previously observed (e.g., included in the Investigator Brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product. In the case of a clinical trial, an unexpected serious adverse event would, for example, be as assessed by the investigator and or the sponsor or authorized person without breaking the blind and would qualify for expedited reporting. An unexpected serious adverse event shall be reported by Transave to the appropriate institutional review board, Regulatory Authority, investigator and PARI.

7.8 **Recalls.**

(a) Each Party shall promptly notify the other Party in writing if any Regulatory Authority or other governmental agency having jurisdiction requests or orders it to conduct a Recall of any Device, or if PARI determines to undertake a Recall of any Device voluntarily. Prior to the beginning of any such Recall, the Parties agree to discuss the Recall process. Promptly after being notified of such Recall, but in no event later than may be required to permit PARI to meet applicable Regulatory Requirements, Transave shall provide PARI with reasonable assistance in connection with such Recall as requested by PARI.

(b) If PARI is required or determines to effect any such Recall, then PARI shall solely manage such Recall and be responsible for (i) the cost of notifying end users; (ii) costs associated with the collection and shipment from end users of the Devices subject to such recall; and (iii) costs of replacing such Devices including the cost of shipping the replacement Devices to the affected end users.

(c) Transave shall promptly notify PARI in writing if any Regulatory Authority or other governmental agency having jurisdiction requests or orders it to conduct a Recall of the Drug Product, or if it determines to undertake a Recall of the Drug Product voluntarily. Prior to the beginning of any such Recall, the Parties agree to discuss the Recall process. Transave shall solely manage such Recall and be responsible for (i) the cost of notifying end users; (ii) costs associated with the collection and shipment from end users of the Drug product subject to such Recall; and (iii) costs of replacing the Drug Product, including the cost of shipping the replacement Drug Product to the affected end users.

Article 8 – Supply of Devices by PARI for Clinical Use

8.1 **Delivery** . PARI agrees to deliver those quantities of Devices and Device Accessories thereof ordered by Transave for clinical trials, FCA (Incoterms 2000) PARI's facilities in Germany, by the delivery dates set forth in a purchase order in accordance with reasonable shipping instructions provided by Transave. The purchase order shall specify the quantity of Device to be supplied, the supply schedule and the study sites, distributors or other site(s) to which delivery shall be made. PARI shall arrange for shipping and insurance, to be paid by Transave, and carry out all customs formalities necessary to export the shipment. The Devices shall be shipped, at Transave's expense, packaged in containers in accordance with the Specifications or as otherwise agreed by the Parties in writing, to Transave or its local country designee, or study site(s) as specified by Transave at the time of ordering the Devices, provided, however, that it will not be required to deliver Devices to more than one (1) centralized location in any given country (except for the United States), unless otherwise agreed by PARI. PARI shall cooperate with Transave, and provide Transave with all necessary documentation and assistance (to the extent PARI has experience as to the importation of Devices into such country), at Transave's expense, with respect to importation of the Devices into any country of the Transave Territory.

8.2 **Payment** . PARI shall submit an invoice to Transave upon shipment of Devices ordered hereunder, reflecting the price therefor as set forth in Exhibit 7.5(a). All invoices shall state the aggregate and unit price for such Devices in a given shipment, plus any insurance, taxes or other costs incident to the purchase or shipment initially paid by PARI but to be borne by Transave hereunder. Other than amounts disputed in good faith, Transave shall pay PARI such invoiced amounts that are due hereunder within (30) days from the date of shipment.

8.3 **Acceptance** .

(a) At the same time it delivers Devices to Transave under Section 8.1, PARI shall deliver to Transave the following documentation: (a) the order number of the delivered Devices and Device Accessories; (b) with respect to the United States only, a Certificate of Conformance, and with respect to the European Union only, a Quality Certificate; and (c) any documentation that PARI customarily includes in shipments of such Device and/or Device Accessories. Transave may, but shall not be obligated to, inspect and test Devices delivered by PARI hereunder. If on such inspection Transave discovers that any Device shipped hereunder fails to conform with the Specifications or otherwise fails to conform to the requirements of this Agreement, Transave may provide written notice to PARI specifying in reasonable detail the manner in which such Device fails to meet the foregoing requirements, and shall promptly send to PARI a representative sample of the nonconforming Device. Transave or its designee shall retain the rejected Devices pending PARI's analysis thereof and the resolution of any disagreement regarding the nonconformance of such Devices.

(b) At its sole cost and expense, PARI shall replace Devices appropriately rejected in accordance with this Section 8.3 by Transave or its designees.

(c) Subject to this Section 8.3 above and 8.4, Devices shall be deemed accepted if no notice to the contrary is received by PARI within thirty (30) days of receipt of such Devices by Transave. It is understood that the warranties given by PARI in Section 8.5 shall survive any failure to reject under this Section 8.3.

8.4 **Latent Defects.** As soon as either Party becomes aware of any defect in Devices delivered by PARI that are not discoverable upon a reasonable inspection or incoming quality assurance testing as set forth in the Specifications, it shall immediately notify the other Party in writing, and the applicable provisions of Section 8.5 shall apply. Notwithstanding the foregoing, in the event that Transave fails to reject a Device within thirty (30) days after it actually becomes aware of any latent defect therein (including, without limitation, by way of written notice from PARI), Transave shall be deemed to have accepted such Device and Section 8.5 shall not apply to such Product with respect to that latent defect only.

8.5 **Replacement.** If any Device fails to work in the patient's possession, Transave shall provide a replacement directly to patient, and PARI shall provide a replacement to Transave within thirty (30) days of notice by Transave, and all replacements covered by PARI's warranty shall be provided at PARI's sole cost and expense subject to PARI's right to dispute such replacement as set forth hereafter. In the event that PARI in good faith does not agree with Transave that any Devices returned by Transave are in fact nonconforming, then within ten (10) business days after receipt of such Devices, PARI shall notify Transave in writing of such disagreement. The Parties shall thereafter attempt in good faith to settle such disagreement by negotiation and consultation between themselves. If the Parties are unable to resolve such disagreement within thirty (30) days of Transave's receipt of PARI's notification thereof, then either Party may within thirty (30) days thereafter (the **"Final Dispute Resolution Period"**) submit the question of nonconformance to an independent third party consultant reasonably acceptable to both Parties. The resolution of the question of nonconformance by such consultant shall be final and binding on both Parties. If such consultant determines that the disputed Devices are nonconforming, PARI shall be responsible for all costs associated with the consultant's services and Transave shall have no payment obligations with respect to such Devices. If such consultant determines that the disputed Devices conform with the applicable requirements therefor, Transave shall be responsible for all costs associated with the consultant's services and for payment for such Devices.

8.6 **Warranties** . PARI represents and warrants that the Devices supplied for clinical trials hereunder (a) shall comply with the Specifications as of the time of first use; (b) shall have no material defects in workmanship upon delivery; and (c) shall, upon shipment to Transave, be free and clear of all security interests, liens and other encumbrances of any kind or character. These warranties, and PARI's obligations hereunder, will survive inspection, test, acceptance and use of the Device.

8.7 **Conflicting Terms and Conditions** . The supply of Devices by PARI to Transave for clinical trial purposes shall be solely in accordance with the terms and conditions of this Agreement. ANY TERMS OR CONDITIONS OF ANY PURCHASE ORDER OR ACKNOWLEDGMENT OR INVOICE GIVEN OR RECEIVED, WHICH ARE ADDITIONAL TO OR INCONSISTENT WITH THIS AGREEMENT SHALL HAVE NO EFFECT, AND SUCH TERMS AND CONDITIONS ARE HEREBY EXCLUDED AND REJECTED BY EACH PARTY.

8.8 **Restrictions of Use.**

(a) Transave will use the Device in compliance with all Applicable Laws and Standards valid in the country Transave intends to conduct clinical trials utilizing the Device, including, for example, those relating to research involving the use of humans or animals and will not engage in any such clinical trials without first obtaining necessary approval from its relevant ethics committee(s) such as, but not limited to, the Institutional Review Board. The Device shall not be used by Transave directly or indirectly for: (i) any purpose other than the clinical trials, or (ii) any profit-making or commercial purpose.

(b) Transave shall retain control of the Device and shall not distribute or release the Device to any person or entity other than Transave's or the clinical trial site's employees, consultants or contractors (**"Transave Representatives"**) and individuals who will be participating in the clinical trials who have a need to access the Device in connection with use of the Device for the clinical trials and who have been advised of Transave's obligations with respect to such Device. Transave shall not allow Transave Representatives to take or send the Device to any other location other than that specified below, unless Transave first obtains PARI's written permission. Transave shall be liable for the use of the Device by Transaction Representatives in violation of this Section 8.8(b).

(c) The Device is to be used in accordance with the terms and conditions of this agreement only by Transave's clinical trial sites as listed in the applicable Work Order by Transave and by Transave Representatives or patients participating in the clinical trials under Transave's control.

(d) Transave shall conduct the clinical trials pursuant to a written protocol (the **"Study Protocol"**). Transave shall provide a synopsis of the Study Protocol to PARI at least thirty (30) days prior to the start of the clinical trial. Following the completion of the clinical trials studies, Transave shall make Commercially Reasonable efforts to retrieve the Devices at Transave's expense and the Devices shall be stored for a limited time as determined by Transave at the clinical trial site and/or Transave's contractors' site. Upon Transave's notice to PARI that the Devices have been retrieved, PARI may arrange for return of the Devices directly with the contractors and/or clinical trial site. PARI shall be solely responsible for the return and/or shipments of the Devices provided that Transave shall pay the reasonable direct shipping costs incurred by PARI in connection therewith.

(e) Transave shall not subject to analysis or have subjected to analysis Devices and/or components constituting Devices received from PARI for the purpose of reverse engineering or in a manner that would reveal material composition or internal design or operation of such sample and/or component or its method of manufacture. Device shall at all times remain the sole and exclusive property of PARI.

8.9 **Commercial Supply.** PARI agrees to deliver, either directly to customers or through a distributor, or to Transave, at Transave's option, on a country by country basis, those quantities of Devices and Device Accessories for commercial use in accordance with the terms set forth in Exhibit 8.9. The Parties shall negotiate in good faith and enter into, in a timely manner, a Commercial Supply Agreement incorporating those terms.

Article 9 – Payment Procedures

9.1 **Invoicing .** PARI shall submit invoices to Transave for the Project Fees owed by Transave for activities under a Work Plan performed by PARI as set forth in the applicable Work Plan. Transave shall pay the undisputed invoiced amounts that are due under this Agreement within thirty (30) calendar days of the date of shipment.

9.2 **Royalties** . Beginning with the First Commercial Sale of a Drug Product and thereafter during the Royalty Term, Transave shall provide PARI with quarterly written royalty reports applicable to royalty payments due to PARI under this Agreement, within sixty (60) days after the last day of each calendar quarter. Each report shall include a summary of the Net Sales, on a country-by-country basis, of the Drug Product that are subject to royalties hereunder during such calendar quarter and a calculation of the royalties due thereon. Simultaneously with the delivery of each such report, Transave shall pay to PARI the total royalties, if any, due to PARI under Article 6 for the period of such report.

9.3 **Annual Minimum Royalty** . For the first four (4) calendar quarter period (**"Year of Sales"**) beginning 180 days after the First Commercial Sale of a Drug Product for use with the Device by Transave, its Affiliates and/or Sublicensees, and for each successive Year of Sales thereafter during the Royalty Term, at the time of its last payment of royalties for the last calendar quarter in such Year of Sales under Section 9.2 above, Transave shall pay PARI the difference, if any, between the royalties actually paid in such Year of Sales and the Annual Minimum Royalty (the " **Minimum Royalty Payment** "). [***]

9.4 **Method of Payment to PARI** . All payments due to PARI under this Agreement shall be made by wire transfer to the bank account designated by PARI. Payments shall be made in US dollars for: Royalties on Net Sales within the US and on Annual Minimum Royalties. Payments shall be made in Euros for: Royalties on Net Sales outside of the US, Milestones and Project Fees. If any currency conversion shall be required in connection with the payment of royalties under Article 6, such conversion shall be made by using the averaged buying and selling exchange rate for such conversion, quoted for current transactions reported in The Wall Street Journal , on the last business day of the calendar quarter immediately prior to such payment.

9.5 **Late Payment** . [***]

9.6 **Transave Books and Records.** Transave shall keep full, true and accurate books and records in accordance with GAAP, which account for the Net Sales of the Drug Product for use with the Device and the royalties due thereon to PARI. PARI, at its own expense, shall have the right during normal business hours on thirty (30) calendar days' prior written notice to Transave and not more than twice in any calendar year to have a nationally recognized independent public accounting firm selected by PARI (and reasonably acceptable to Transave) examine such books and records for the purpose of verifying the royalty payments due to PARI under this Agreement. Such accounting firm shall execute and deliver to Transave a standard confidentiality agreement and shall not disclose to PARI any information relating to Transave's business, except whether Transave's royalty payments are correct or incorrect, and if incorrect, the specific details concerning any discrepancies and the amounts of the royalties due hereunder pursuant to Section 6.1 of this Agreement. If such examination reveals a discrepancy, Transave shall promptly pay to PARI any additional royalty owed to PARI. In addition, if the discrepancy is greater than [***] in PARI's favor, Transave shall also promptly reimburse PARI for the fees and costs of the independent public accounting firm.

9.7 **PARI Books and Records** . PARI shall keep full, true and accurate books and records in accordance with GAAP, which account for the activities under a Work Plan performed by PARI and the Project Fees due to PARI thereon. Transave, at its own expense, shall have the right during normal business hours on thirty (30) calendar days' prior written notice to PARI and not more than twice in any calendar year to have a nationally recognized independent public accounting firm selected by Transave (and reasonably acceptable to PARI) examine such books and records of PARI for the purpose of verifying the Project Fees invoiced to Transave over the preceding twelve (12) month period. Such accounting firm shall execute and deliver to PARI a standard confidentiality agreement and shall not disclose to Transave any information relating to PARI's business, except whether PARI's invoices are correct or incorrect, and if incorrect, the specific details concerning any discrepancies and the amounts of the Project Fees due hereunder. If such examination reveals a discrepancy, PARI shall promptly pay to Transave any additional amount owed to Transave. In addition, if the discrepancy is greater than [***] in Transave's favor, PARI shall also promptly reimburse Transave for the fees and costs of the independent public accounting firm.

Article 10 – Prosecution, Marking, Enforcement and Defense

10.1 **Patent Prosecution.** During the term of this Agreement, PARI shall promptly notify Transave in writing of the filing or issuance of any patent applications or patents within the PARI Intellectual Property licensed to Transave pursuant to this Agreement that include subject matter related to the Project, or the Device.

10.2 **Patent Marking** . Each Party agrees to mark all Products in accordance with the applicable statutes or regulations in the country or countries of manufacture and sale thereof. For such purposes, each Party shall provide the other Party with written notice of all of its patent numbers applicable to the Products.

10.3 **Patent Enforcement** .

(a) **Enforcement** . Subject to the provisions of Section 3.6 and this Section 10.3, in the event that Transave or PARI reasonably believes that any Patent Rights within the PARI Intellectual Property are being infringed or misappropriated in the Transave Field by a third party, such Party shall promptly notify the other Party. Transave shall have the initial right (but not the obligation) to bring and/or control any enforcement action directed to the Drug Product, and PARI shall have the initial right (but not the obligation) to bring and/or control any enforcement action directed to the Device, including specific design elements of the hardware apparatus or the software of the Device.

(b) **Backup Right to Enforce** . In the event PARI does not initiate such an enforcement action within one hundred and eighty (180) days after a request by Transave to initiate an enforcement action against an alleged infringement, or notifies Transave at any time that it does not desire to enforce or defend such Patent Rights with respect to such alleged infringement, then Transave shall have the right (but not the obligation) to enforce or defend against such alleged infringement, provided that any settlement of such infringement shall be subject to the approval of both Parties.

(c) **Cooperation.** The Party controlling the enforcement action shall keep the other Party reasonably informed of the progress thereof, and the other Party shall have the right to participate with counsel of its own choice at its own expense, and shall reasonably cooperate with the Party initiating the enforcement action (including joining as a party plaintiff to the extent necessary and requested by the other Party) at the expense of the Party requesting such cooperation.

(d) **Allocation of Recoveries** . Unless otherwise agreed, all amounts recovered in an enforcement action, after reimbursing each Party for its costs and expenses incurred therein, shall be shared between the Parties by the proportion and up to the extent of any damages established in such enforcement action, including but not limited to lost profits or royalties. The balance, if any, shall be retained by the Party that initiated the enforcement action.

10.4 **Defense of Third Party Infringement Claims** . If the development, manufacture, sale, offer for sale, importation, exportation or use of the Drug Product or the Device results in a claim alleging patent infringement against either Party (or its respective Affiliates or permitted Sublicensees), such Party shall promptly notify the other Party hereto in writing. Subject to Sections 3.5, 13.1 and 13.2, (i) Transave shall have the exclusive right to defend and control the defense of any infringement claim pertaining to primarily the Drug Product, and (ii) PARI shall have the exclusive right to defend and control the defense of any infringement claim pertaining to primarily the Devices and/or any component of the foregoing, each Party using counsel of its own choice as applicable; provided, however, that the other Party shall be kept informed of all material developments in connection with any such claim.

Article 11 – Confidentiality

11.1 **Non-use and Non-disclosure Obligations** . Each of PARI and Transave shall use any Confidential Information received by it from the other Party solely in connection with performance of their respective obligations, rights and other permitted activities under, and other purposes of, this Agreement and shall not disclose such Confidential Information to any Third Party, without the prior written consent of the other Party. Notwithstanding the foregoing and anything to the contrary in this Agreement, Transave shall not share with or provide to any PARI Competitor any of the PARI Confidential Information. These obligations shall survive the termination of this Agreement for a period of ten (10) years. For purposes of this Agreement, "Confidential Information" means the confidential or proprietary scientific, regulatory, clinical, technical or business information, materials and technologies of a Party disclosed or learned under this Agreement, including the Work Plans and any information exchanged prior to the Effective Date, whether in written, oral, electronic, photographic, magnetic or other form. For clarity, the Data and Intellectual Property owned by a Party pursuant to this Agreement shall be deemed the Confidential Information of such Party. Confidential Information shall exclude any information that:

11.1.1 is known by the receiving Party without restriction at the time of receipt and not through a prior disclosure by the disclosing Party;

11.1.2 is at the time of disclosure or thereafter becomes published or otherwise part of the public domain through no breach of this Agreement by the receiving Party;

11.1.3 is subsequently disclosed to the receiving Party without restriction by a third party having the right to make such a disclosure; or

11.1.4 is developed by the receiving Party independently of Confidential Information received by it from the disclosing Party hereunder.

11.2 **Required Disclosure** . In order to provide the disclosing Party an opportunity to seek a protective order or the like with respect to certain Confidential Information, the receiving Party may disclose Confidential Information to the extent that it is required by law or order of any governmental authority or agency, including the Securities and Exchange Commission, to be disclosed by a Party; provided that the receiving Party, using good faith efforts, shall apply for confidential treatment of such Confidential Information, shall provide the other Party a copy of the confidential treatment request far enough in advance, if possible, of its filing to give the other Party a meaningful opportunity to comment thereon, and shall incorporate in such confidential treatment request any reasonable comments of the other Party, in each case to the fullest extent permitted under applicable laws, rules or regulations.

11.3 **Permitted Disclosure** . Notwithstanding Section 11.1, Confidential Information provided under this Agreement may be disclosed to employees, agents, consultants, or suppliers of the receiving Party or professional advisors (or permitted Sublicensees, in the case of Transave), but only to the extent permitted or required to accomplish the purposes of, or to perform its obligations, rights and other permitted activities under, this Agreement; provided that such employees, agents, consultants, professional advisors, permitted Sublicensees or suppliers shall also agree to appropriate and comparable confidentiality and non-use provisions. Notwithstanding the foregoing and anything to the contrary in this Agreement, Transave shall not share with or provide to any PARI Competitor any of the PARI Confidential Information. The receiving Party shall be responsible for any breaches of this Agreement by its employees, agents, consultants, or suppliers. In addition, a Party may disclose Confidential Information provided under this Agreement by the other Party to any governmental authority in order to prosecute or maintain any Intellectual Property or any Regulatory Authority to obtain approval to market a Product, but such disclosure may be made only to the extent necessary to pursue such prosecution or maintenance or to obtain such approval, all to the extent permitted or required to accomplish the purposes of this Agreement.

11.4 **Return** . Upon the termination of this Agreement, all Confidential Information of the disclosing Party in the receiving Party's possession will be returned to the disclosing Party (or destroyed by the receiving Party, with written confirmation of such destruction), and the receiving Party will make no further use thereof. Notwithstanding the foregoing, the receiving Party may retain one copy of the Confidential Information of the disclosing Party solely for archival purposes to ensure compliance with the provisions of this Article 11 or with the requirements of Regulatory Authorities.

11.5 **Publicity**

(a) **Press Releases** . Neither Party shall use the other Party's name in any press release, publicity, advertising nor other official form of public disclosure without such other Party's prior written consent, which consent shall not be unreasonably withheld, delayed or conditioned. Notwithstanding the foregoing, Transave shall have the right to issue a press release or make other public disclosures announcing milestones or other significant progress pertaining to its development and/or commercialization of Drug Products and the Device, provided that if issued without the prior written consent of PARI, such press releases shall not disclose any Confidential Information of PARI hereunder and shall at all times be consistent with the last two sentences of this Section 11.5(a). In addition, once any subject matter has been publicly disclosed in accordance with this Section 11.5, no further consent from either Party will be needed for further disclosures of such subject matter. Notwithstanding the above, in all press releases, public statements, publicity, advertising or other public disclosure pertaining to the development of the Drug Product and the Device, Transave shall always give appropriate attribution to PARI's role(s) in the Project contemplated herein. Notwithstanding the foregoing, all press releases and similar disclosures issued by Transave shall always contain the language set forth on Exhibit 11.5 attached hereto, as such Exhibit may be amended from time to time by PARI.

(b) **Terms of this Agreement** . Neither Party shall disclose the terms of this Agreement to any third party, without the prior written consent of the other Party, which consent shall not be unreasonably withheld, except as required by any law or regulation or in connection with any financing transaction, or bona fide (good faith) due diligence inquiry, subject to such parties agreeing to comparable confidentiality and non-use provisions as set forth in this Article 11 and Transave being responsible for any breaches by such third party (ies). Notwithstanding the foregoing, the disclosure of any terms of this Agreement to a PARI Competitor shall require the prior written consent of PARI, to be granted in its sole discretion.

(c) **Publications.** Transave shall consult with PARI prior to submission of any manuscript for publication or making any public presentation, including speeches and conference posters, pertaining to the activities conducted under a Work Plan. Such consultation shall include providing a copy of the proposed manuscript or presentation reasonably in advance of the proposed date of submission of such manuscript to a publisher or the proposed date of presentation, giving due consideration to PARI's comments as to such publication or presentation, and as requested by PARI removing any Confidential Information of PARI therefrom. Notwithstanding the above, in all press releases, public statements, publicity, advertising or other public disclosure pertaining to the development of the Drug Product and/or the Device, Transave shall always give appropriate attribution to PARI's role(s) in the Project contemplated herein. PARI shall not publish or make any presentations regarding any Drug Product, Transave Intellectual Property, Transave Confidential Information or the activities conducted under a Work Plan except with the prior written consent of Transave. Transave shall not publish or make any presentations that incorporate PARI Intellectual Property, Project Intellectual Property, PARI Confidential Information or the activities conducted under a Work Plan except with the prior written consent of PARI.

(d) **Required Disclosures** . Notwithstanding Section 11.5(a) through (c) above, either Party may make such disclosures relating to this Agreement, the terms and conditions hereof or the activities hereunder, as such Party deems to be required by law or in any filings with governmental entities or national securities exchanges, provided that such Party shall use good faith efforts to apply for confidential treatment of this Agreement and redact such portions of this Agreement as reasonably requested by the non-disclosing Party, in each case to the fullest extent permitted under applicable laws, rules or regulations.

Article 12 – Representations and Warranties

12.1 **PARI Representations and Warranties** . PARI represents, warrants and covenants that, other than as set forth on Exhibit 12.1 attached hereto:

(a) PARI is a corporation duly organized, existing and in good standing under the laws of Germany, with full right, power and authority to enter into and perform this Agreement;

(b) the execution, delivery and performance of this Agreement does not conflict with, violate or breach any agreement to which PARI is a party, any court order to which PARI is a party or subject to or PARI's organizational documents;

(c) this Agreement has been duly executed and delivered by PARI and is a legal, valid and binding obligation enforceable against PARI in accordance with its terms subject to applicable bankruptcy, insolvency, reorganization, arrangement, moratorium and other laws relating to or affecting creditors' rights generally and equitable principles;

(d) as of the Effective Date: (i) PARI owns or has the right to license to Transave all of the PARI Intellectual Property, and the PARI Intellectual Property includes all Patent Rights and Know-How in which PARI has a right or license that may be applicable to the Device in the Transave Field; (ii) PARI has the right to grant the licenses and rights set forth in this Agreement; and (iii) to the best of PARI's knowledge, patents within the PARI Intellectual Property are valid and enforceable, and are not known to be infringed by any third party in the Transave Territory;

(e) as of the Effective Date, to the best knowledge of PARI, PARI has not intentionally withheld from Transave any material information related to the Device; to the best knowledge of PARI, the information relating to the Device provided by PARI to Transave does not contain any misstatement of a material fact nor omit to state any material fact required to make such information as of the date of submission to Transave not materially misleading;

(f) PARI shall perform its activities under a Work Plan in a competent and professional manner, in accordance with a Work Plan, Applicable Laws and Standards and any reasonable instructions provided by Transave to PARI; and

(g) to PARI’s knowledge as of the Effective Date, the Device does not infringe, misappropriate or otherwise violate any patent or other Intellectual Property Rights of any Third Party.

12.2 **Transave Representations and Warranties .** Transave represents, warrants and covenants that:

(a) Transave is a corporation duly organized, existing and in good standing under the laws of the State of Delaware, with full right, power and authority to enter into and perform this Agreement;

(b) the execution, delivery and performance of this Agreement does not conflict with, violate or breach any agreement to which Transave is a party, any court order to which Transave is a party or subject to, or Transave' certificate of incorporation or bylaws;

(c) this Agreement has been duly executed and delivered by Transave and is a binding obligation enforceable against Transave in accordance with its terms subject to applicable bankruptcy, insolvency, reorganization, arrangement, moratorium and other laws relating to or affecting creditors' rights generally and equitable principles;

(d) as of the Effective Date, to the best knowledge of Transave, Transave has not intentionally withheld from PARI any material information related to the Drug Product; to the best knowledge of Transave, the information relating to the Drug Product provided by Transave to PARI does not contain any misstatement of a material fact nor omit to state any material fact required to make such information as of the date of submission to PARI not materially misleading;

(e) as of the Effective Date: (i) Transave owns or has the right to license to PARI all of the Transave Intellectual Property, and the Transave Intellectual Property includes all Patent Rights and Know-How in which Transave has a right or license that may be required for PARI to perform its obligations under this Agreement; (ii) Transave has the right to grant the licenses and rights set forth in this Agreement; and (iii) to the best of Transave's knowledge, patents within the Transave Intellectual Property are valid and enforceable, and are not known to be infringed by any third party in the Transave Territory; and

(f) to Transave's knowledge as of the Effective Date, the pulmonary administration of Drug Product through a Nebulizer does not infringe any patent or other intellectual property rights of any third party.

12.3 **Disclaimer.** EXCEPT AS OTHERWISE EXPRESSLY SET FORTH IN THIS ARTICLE 12 OR IN SECTION 8.6 ABOVE, NEITHER PARTY MAKES ANY REPRESENTATIONS OR EXTENDS ANY WARRANTIES TO THE OTHER PARTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, REGARDING PATENT RIGHTS, KNOW-HOW OR DATA INCLUDING, BUT NOT LIMITED TO, WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NONINFRINGEMENT, NOR VALIDITY.

12.4 **Limitation of Liability** . NEITHER PARTY SHALL BE LIABLE TO THE OTHER PARTY UNDER ANY CIRCUMSTANCES OR ANY LEGAL OR EQUITABLE THEORY, WHETHER IN CONTRACT, STRICT LIABILITY OR OTHERWISE, FOR ANY INDIRECT, INCIDENTAL, PUNITIVE OR CONSEQUENTIAL DAMAGES OR DAMAGES FOR LOST PROFITS ARISING OUT OF OR RELATED TO THIS AGREEMENT, EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. THESE LIMITATIONS SHALL APPLY NOTWITHSTANDING ANY FAILURE OF ESSENTIAL PURPOSE OR ANY LIMITED REMEDY.

Article 13 – Indemnification; Insurance

13.1 [***]

13.2 **Indemnification of PARI** . Transave shall at all times be responsible for, and shall defend, indemnify and hold PARI, its Affiliates, directors, officers, employees, agents and representatives harmless from and against any and all losses, claims, lawsuits, proceedings, expenses, recoveries and damages, including reasonable legal expenses, costs and attorneys fees, arising out of: (i) any product liability claim or lawsuit by a third party directly arising from the Drug Product; (ii) any claim of infringement of any patent rights, trade secrets rights or other intellectual property rights of a third party arising from the Drug Product or the manufacture thereof; (iii) Transave's material breach of any representation, warranty or covenant given in this Agreement by Transave; and (iv) any negligent conduct or willful misconduct by Transave in performance under this Agreement; provided however, that: (a) PARI gives Transave prompt notice of any such claim or lawsuit; (b) Transave has the right to compromise, settle or defend such claim or lawsuit; and (c) PARI, at the expense of Transave, cooperates with Transave in the defense of such claim or lawsuit. PARI, at its expense, may participate in the defense of any such claim or lawsuit.

13.3 **Insurance .** During the term of this Agreement and for a reasonable period of time thereafter, each Party or its Affiliates, shall maintain appropriate product liability insurance with respect to any clinical trials, manufacturing, development, sales, marketing, distribution and promotion activities performed by it hereunder. Each party shall, upon request of the other party, provide the requesting party with a certificate of insurance evidencing coverage under the foregoing policies of insurance, along with any amendments and revisions thereto. PARI shall be (i) named as an additional insured on any such policies maintained hereunder by Transave, and (ii) also added by endorsement on such policies. With respect to the U.S., Transave shall be (i) named as an additional insured on any such policies maintained hereunder by PARI's Affiliate, PRE Holding, Inc., and (ii) also added by endorsement on such policies of PRE Holding, Inc.

Article 14 – Dispute Resolution

PARI and Transave shall endeavor to resolve any claim or controversy arising out of the threatened breach, breach, enforcement, interpretation, termination or validity of this Agreement informally by good faith negotiation between the senior executives, officers or management of PARI and Transave. Either Party may give the other Party written notice of any claim or controversy not resolved in the normal course of business (the " **Disputing Party Notice** "). Within thirty (30) calendar days after the delivery of the Disputing Party Notice, the receiving Party shall submit to the other Party a written response (the " **Response** "). The Disputing Party Notice and Response shall include a statement of each Party's position and a summary of the arguments supporting that position. Within sixty (60) days after the Disputing Party Notice, such designated senior executives, officers or management of PARI and Transave shall meet at a mutually acceptable time and place and thereafter as often as they reasonably deem necessary to attempt to resolve the claim or controversy. All negotiations pursuant to this Section 14 are confidential and without prejudice and shall be treated as compromise and settlement negotiations for purposes of applicable rules of evidence. Any claim or controversy unresolved after application of this Article 14 shall be subject to Section 16.3 of this Agreement.

Article 15 – Term and Termination

15.1 **Term** . The term of this Agreement is effective as of the Effective Date as first written above, and except as otherwise terminated in accordance with this Article 15, shall continue in full force and effect until the expiration of the final Royalty Term in the last country in which Drug Product is sold.

15.2 **Termination by Either Party** . Subject to force majeure provisions set forth in Section 16.10 of this Agreement, each Party shall have the right to terminate this Agreement upon written notice, (i) in the event the other Party is in material breach of this Agreement, and does not cure such breach within ninety (90) days after written notice thereof, specifying in reasonable detail the breach; provided, however, that for payments due pursuant to this Agreement, the cure period shall be thirty (30) days after receipt of written notice of such past due payment; provided, however, that immediately in the event the other Party initiates a voluntary proceeding under the U.S. Bankruptcy Code, or any equivalent proceeding under the laws of any other jurisdiction; or in the event such Party becomes the subject of an involuntary proceeding under the U.S. Bankruptcy Code, or any equivalent proceeding under the laws of any other jurisdiction, and such proceeding is not dismissed or stayed within ninety (90) days of its commencement.

15.3 **Termination by Transave.** Transave shall have the right to terminate this Agreement upon written notice in the event that (i) Transave receives a negative review or negative comments from the FDA, EMEA or another Regulatory Authority which indicates that Transave will be unable to obtain regulatory approval of an MAA for the Drug Product for use with the Device solely due to the Device not substantially meeting the Specifications, (ii) PARI is unable (subject to the force majeure provisions set forth in Section 16.10 of this Agreement) or unwilling to supply Devices to Transave in connection with clinical trials in accordance with the provisions of Article 8 that would prevent Transave from timely completing its Phase II and Phase III Trials, [***]

15.4 **Termination by PARI.** PARI shall have the right to terminate this Agreement upon written notice in the event that (i) Transave assigns or otherwise transfers this Agreement to a third party that does not execute a written undertaking agreeing to assume all of Transave's rights and obligations set forth in this Agreement and otherwise abide by the terms and conditions of this Agreement, [***] (v) the licenses granted to Transave under this Agreement have been terminated pursuant to: (x) Section 6.3(b) for both CF and Bronchiectasis; or (y) Sections 7.1(b) and 7.2(a) and the Parties have not entered into an additional agreement for a Secondary Indication in accordance with the provisions of Section 2.6.

15.5 **Effects of Expiration or Termination**

(a) **Accrued Obligations** . Expiration or sooner termination of this Agreement shall not release either Party hereto from any liability which at the time of such expiration or termination has already accrued to such Party, nor preclude either Party from pursuing any rights and remedies it may have hereunder or at law or in equity.

(b) **Sublicenses.** Upon the termination of this Agreement for any reason, any sublicenses granted by Transave hereunder shall survive (unless specified otherwise in the applicable sublicense agreement), provided that, upon request by PARI, each Sublicensee promptly agrees in writing to be bound by the applicable terms of this Agreement, and agrees to pay directly to PARI the same amounts that would have been due to PARI from Transave under this Agreement with respect to such sublicense, had the Agreement not terminated.

(c) **Return of Rights** . Except as reasonably necessary for surviving rights or obligations under this Article 15, (i) all of PARI's and Transave's license rights under Articles 3.1 and 4 shall terminate, and (ii) each of Transave and PARI shall promptly return all Confidential Information then in possession in accordance with Section 11.4 of this Agreement.

(d) **Survival.** Articles 1, 9, 11, 13, 14, 15 and 16, Sections 2.6, 3.2, 3.4, 3.6, 8.2, 8.8, 10.3 for cases initiated before termination, 10.4 (except for the proviso at the end of the paragraph, which shall not survive), 12.4 and 15.5 shall survive any expiration or termination of this Agreement and Sections 8.4 and 8.6 shall survive the termination of this Agreement for a period of twelve (12) months. Except as set forth in this Section 15.5, all other Articles and Sections of this Agreement shall terminate upon termination of this Agreement.

Article 16 – Miscellaneous

16.1 **Entire Agreement .** This Agreement, which includes the Exhibits attached hereto, contains the entire agreement between PARI and Transave with respect to the transactions contemplated by this Agreement and supersedes all prior agreements, arrangements or understandings with respect thereto.

16.2 **Notices .** Every notice, election, demand, consent, request, approval, report, offer, acceptance, certificate, or other communication required or permitted under this Agreement or by applicable law shall be in writing and shall be deemed to have been delivered and received (a) when personally delivered, (b) on the seventh (7th) business day after which sent by registered or certified mail, postage prepaid, return receipt requested, (c) on the date on which transmitted by facsimile or other electronic means generating a receipt evidencing a successful transmission (provided that, on that same date, a copy of such notice is sent by registered or certified mail, postage prepaid, return receipt requested), or (d) on the third (3rd) business day after the business day on which deposited with a regulated public carrier (e.g., Federal Express) for overnight delivery (receipt verified), freight prepaid, addressed to the Party for whom intended at the mailing address or facsimile number set forth below, or such other mailing address or facsimile number, notice of which is given in a manner permitted by this Section 16.2:

If to Transave:	Transave, Inc 11 Deer Park Drive, Suite 117 Monmouth Jct., New Jersey 08852 United States of America Phone: [***] Attn: [***] Fax: [***]
with a copy to:	Gunderson Dettmer Stough, Villeneuve Franklin & Hachigian, LLP 610 Lincoln Street Waltham, MA 02451 Phone: [***] Attn: [***] Fax: [***]
If to PARI:	PARI Pharma GmbH Moosstrasse 3, D-82319 Starnberg, Germany Phone: [***] Fax: [***] Attn: [***] Title: [***]

with a copy to: McGuireWoods LLP
One James Center
901 East Cary Street
Richmond, Virginia 23219-403
Attn: [***]
Fax: [***]

Any Party may by such notice change the address to which notice or other communications to it are to be delivered or mailed.

16.3 **Choice of Law .** This Agreement is construed in accordance with, and its performance is governed by, the laws of State of New York, excluding its or any other jurisdiction's choice of law principles. Any dispute arising hereunder shall be brought exclusively in the state or federal courts located in the State of New York in the division of Manhattan. The Parties hereby consent to the exclusive jurisdiction and venue of such courts and waive any objections to the jurisdiction and venue thereof. In the event of any conflict between US and foreign laws, regulations and rules, US laws, regulations and rules shall govern. The UN Convention on contracts for the International Sale of Goods shall not apply to this Agreement.

16.4 **Assign ment.** This Agreement shall not be assignable by either Party without the prior written consent of the other Party, which consent shall not be unreasonably withheld, delayed or conditioned, except that without consent either Party may assign or transfer the rights and obligations of this Agreement to any Affiliate or to any successor to its business that related to the subject matter of this Agreement (whether by sale of assets or equity, merger, consolidation or otherwise) provided, however, that such assignment or transfer by Transave to a PARI Competitor shall require the prior written consent of PARI, to be granted in its sole discretion. This Agreement shall inure to the benefit of and be binding upon the Parties hereto and their respective successors and permitted assigns. Any assignment in contravention of the foregoing shall be null and void.

16.5 **Waivers and Amendments .** Any waiver of any term or condition of this Agreement, or any amendment or supplementation of this Agreement, shall be effective only if in writing signed by the Parties. A waiver of any breach or failure to enforce any of the terms or conditions of this Agreement shall not in any way affect, limit or waive a Party's rights hereunder at any time to enforce strict compliance thereafter with every term or condition of this Agreement.

16.6 **Severability** . Both Parties hereby expressly state that it is the intention of neither Party to violate any law. If any of the provisions of this Agreement are held to be void or unenforceable, then such void or unenforceable provisions shall be replaced by valid and enforceable provisions which will achieve as far as possible the economic business intentions of the Parties.

16.7 **Construction.** The article and section headings contained in this Agreement are for the purpose of convenience and are not intended to define or limit the contents of such sections. Unless the context of this Agreement clearly requires otherwise, (a) references to the plural include the singular, the singular the plural, the part the whole, (b) references to any gender include all genders, (c) "or" has the inclusive meaning frequently identified with the phrase "and/or," (d) "including" has the inclusive meaning frequently identified with the phrase "including but not limited to" or "including without limitation", and (e) references to "hereunder" or "herein" relate to this Agreement.

16.8 **Counterparts .** This Agreement may be signed in one or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement may be executed in one or more counterparts, each of which shall be an original, but taken together constituting one and the same instrument. Execution of a facsimile copy shall have the same force and effect as execution of an original, and a facsimile signature shall be deemed an original and valid signature.

16.9 **Further Assurances .** Upon the reasonable request of either Party, the other Party shall execute any additional certificates or other documents that may be reasonably necessary to fully implement this Agreement.

16.10 **Force Majeure .** No failure or omission by either Party in the performance of any obligation of this Agreement shall be deemed a breach of this Agreement or create any liability if the same shall arise from any cause or causes beyond the reasonable control of such Party including, but not limited to the following which, for the purposes of this Agreement, shall be regarded as beyond the control of the Party in question: (a) any act or omission of any government; (b) any future rule, regulation or order issued by any governmental authority or by any officer, department, agency, or instrumentality thereof which makes such performance impossible or commercially unreasonable; or (c) any Act of God; fire; storm; flood; earthquake; accident; war; terrorism; rebellion; insurrection; riot; invasion; strike; and lockout.

16.11 **Compliance with Applicable Law s and Standards.** In conducting any activity under this Agreement or in connection with the development, manufacture, use, sale, offer for sale, importation and exportation of the Products, PARI and Transave shall comply with all Applicable Laws and Standards including, but not limited to, all import and export regulations of the applicable authorities in the Transave Territory.

16.12 **Relationship of the Parties .** In making and performing this Agreement, the Parties are acting, and intend to be treated, as independent entities and nothing contained in this Agreement shall be construed or implied to create an agency, partnership, joint venture, or employer and employee relationship between or among any of the Parties. Except as otherwise provided herein, no Party may make any representation, warranty or commitment, whether express or implied, on behalf of or incur any charges or expenses for or in the name of any other Party. No Party shall be liable for the act of any other party unless such act is expressly authorized in writing by such Party.

16.13 **Choice of Language .** This Agreement, originally written in the English language, shall be governed by the English language. In the event any dispute arises with respect to this Agreement, the meanings of all terms and provisions of this Agreement shall be interpreted in their original English form. The governing language of all correspondence related to reporting, negotiation, disputes, arbitration and notice requirements shall be the English language. The Parties shall bear their own expenses for having text or other communications translated into the English language.

16.14 **Injunctive Relief** . Each Party hereto understands and agrees that the unauthorized use and the threatened use or disclosure of the other Party's Intellectual Property, Project Intellectual Property or Confidential Information may cause irreparable, competitive harm and significant injury. Therefore, in the event of such unauthorized use or disclosure, in addition to all rights and remedies available to it at law and in equity, including the collection of damages, each Party hereto shall be entitled to seek immediate injunctive relief as is necessary to restrain any continuing or further breach of this Agreement without sharing or proving any actual damages sustained by such Party and without requirement of bond.

IN WITNESS WHEREOF, the Parties hereby have executed this Agreement, as of the Effective Date.

Transave:		PARI:	
TRANSAVE, INC.		**PARI PHARMA GMBH**	
By:	/s/ Tim Whitten	By:	/s/Martin Knoch
Name:	Tim Whitten	Name:	Martin Knoch
Title:	CEO/President	Title:	President
Date:	4/25/08	Date:	4/30/08

EXHIBIT 1.35

[***]

EXHIBIT 1.38

[***]

EXHIBIT 1.38A

[***]

EXHIBIT 2.2

[***]

EXHIBIT 4.1

[***]

EXHIBIT 7.5(a)

[***]

EXHIBIT 7.5(b)

[***]

EXHIBIT 7.6(a)

[***]

EXHIBIT 8.9

[***]

EXHIBIT 11.5

[***]

EXHIBIT 12.1

[***]

AMENDMENT NO. 1
TO LICENSE AGREEMENT BETWEEN
TRANSAVE, INC. AND PARI PHARMA GMBH

This first amendment ("Amendment No. 1") effective the 24 th day of June, 2009

("Effective Date") is made to the License Agreement dated and effective the 25 th of April 2008 ("Agreement") 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 with registered Offices at 11 Deer Park Drive, Suite 117, Monmouth Junction, NJ 08852, United States of America ("Transave"). PARI and Transave shall be referred to collectively as the " **Parties** ."

WHEREAS Transave and PARI desire to add to the Transave Field a Secondary Indication, Non-tuberculosis Mycobacteria infections, pursuant to Sections 1.50 and 2.6 of the Agreement; and

WHEREAS Transave and PARI desire to amend the Agreement to provide terms for the added indication.

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 to amend the Agreement as follows:

1. Section 1,54, line 2, delete "cystic fibrosis (CF) and/or bronchiectasis" and insert --cystic fibrosis (CF), bronchiectasis and/or Non-tuberculosis Mycobacteria infections--.

2. Section 2.5, line 5, delete "CF, Bronchiectasis or such Secondary Indication" and insert -- CF, Bronchiectasis, Non-tuberculosis Mycobacteria infections or any other Secondary Indication,

3. Section 4.1, line 9, change "2.5.2" to –2.5--.

4. Section 4.2(a),
   line 3, delete "CF and/or Bronchiectasis" and insert --CF, Bronchiectasis and/or Non-tuberculosis Mycobacteria infections--; and
   line 26 (last line), delete "CF and Bronchiectasis" and insert --CF, Bronchiectasis and Non-tuberculosis Mycobacteria infections--.

5. Section 4.2(b), delete "PARI's obligations under Section 4.2(a) shall be conditioned upon Transave complying with its diligence obligations as set forth in Sections 7.1 and 7.2." and insert ---PARI's obligations under Section 4.2(a) with respect to CF, bronchiectasis and Non-tuberculosis Mycobacteria infections, respectively, shall be conditioned upon Transave complying with its diligence obligations as set forth in Sections 7.1, 7.2 and 7.2A, respectively.--.

6. Section 6.3, first paragraph,
   line 3, before “in the event Transave” insert --(a)--; and
   line 6, after “in effect” insert --, and (b) in the event Transave has permanent!), discontinued to Exploit the Drug Product for CF in accordance with Section 7.1(a) and discontinued to Exploit the Drug Product for Bronchiectasis, then the Annual Minimum Royalty shall no longer be applicable for the Drug Product for CF or Bronchiectasis but the obligation to pay Annual Minimum Royalties for the Drug Product shall apply to Non-tuberculosis Mycobacteria infections--.

7. Section 6.3(b), lines 5-6, delete “CF or Bronchiectasis” and insert --CF, Bronchiectasis or Non-tuberculosis Mycobacteria infections--.

8. Section 7.2(b), line 4, delete “CF or any Secondary Indication” insert --CF, Non- tuberculosis Mycobacteria infections or any other Secondary Indication--.

9. Before Section 7.3, insert a new section 7.2A as follows:

“ 7.2A **Transave Development and Commercialization Diligence for Non-tuberculosis Mycobacteria Infections.**

(a) The Parties agree that Transave will use Commercially Reasonable Efforts to meet the following milestone with respect to Non-tuberculosis Mycobacteria infections:

Milestone Activity	**Milestone Deadline**
1. **Diligence Milestone 1:** Last patient to complete the Phase II Trial for Non-tuberculosis Mycobacteria infections	[***]
2. **Other Diligence Milestones:** see below	

Within one hundred eighty (180) days following the final results of the Phase II Trial for Non-tuberculosis Mycobacteria infections, the Parties, acting in good faith, will negotiate additional milestones that meet reasonable industry standards. If no additional milestones are agreed to within such time period, and the lack of milestones is not mutually agreed by both parties, then at PARI’s option, PARI may by providing prompt written notice to Transave, (1) make the license granted to Transave under this Agreement non-exclusive and PARI’s non- compete obligations set forth in Section 4.2 shall terminate or (ii) terminate the license granted to Transave under this Agreement, in each case solely with respect to Non-tuberculosis Mycobacteria infections.

If Transave fails to meet a milestone within the applicable time period, other than any failure resulting from a breach of this Agreement by PARI, then, subject to the provisions of Section 7.3, PARI shall have the option to render Transave's license hereunder non-exclusive solely with respect to Non-tuberculosis Mycobacteria infections and to terminate its obligation not to compete with Transave in Non-tuberculosis Mycobacteria infections as set forth in Section 4.2 of this Agreement. Such option must be exercised by sending the Diligence Termination Notice to Transave, and shall become effective on the thirtieth (30 th) day following the date of the Diligence Termination Notice. If such milestone is still not met within twelve (12) months of the applicable time period, other than any failure resulting from a breach of this Agreement by PARI, then, subject to the provisions of Section 7.3, PARI shall have the option to terminate the license granted to Transave under this Agreement with respect to Non-tuberculosis Mycobacteria infections only by providing written notice thereof to Transave.

(b) For the avoidance of doubt, subject to the provisions of Section 7.2A(a), nothing in this Agreement shall impart any obligation on Transave to pursue the indication of Non-tuberculosis Mycobacteria infections, and Transave's activity or lack of activity with respect to Non-tuberculosis Mycobacteria infections shall not affect in any way Transave's rights in and to CF, Bronchiectasis or any other Secondary Indication.

10. Section 7.3, line 2,: delete "Section 7.1(b) and/or 7.2(a)" and insert --Section 7.1(b), 7.2(a) and/or 7.2A(a)--.

11. Section 15.4,
    line 10, delete "Section 6.3(b) for both CF and Bronchiectasis" and insert -- Section 6.3(b) for CF, Bronchiectasis and Non-tuberculosis Mycobacteria infections--; and
    line 11, after "7.1(b) and 7.2(a)" insert -- and 7.2A(a)--.

IN WITNESS WHEREOF, the Parties have executed this Amendment No.1 as of the Effective

Date indicated above.

TRANSAVE, INC.

By: /s/ Tim Whitten

Tim Whitten
President and CEO

Date: July 14, 2009

PARI PHARMA GMBH

By: /s/ Martin Knoch

Martin Knoch
President

Date: July 6, 2009

ASSIGNMENT AND AMENDMENT NO. 2
TO LICENSE AGREEMENT BETWEEN
TRANSAVE, INC. AND PARI PHARMA GMBH

This assignment and second amendment ("Amendment No, 2") effective the 22 nd day of December, 2010 ("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 ("Transave Inc."), as amended by Amendment No. 1 the 24 th day of June 2009 (collectively, the "Agreement"), is entered into between PARI, Transave, LLC, a Delaware limited liability company and successor to Transave, Inc. ("Transave LLC") and Insmed Incorporated, a Virginia corporation with registered Offices at 8720 Stony Point Parkway, Suite 200, Richmond, VA 23235 ("Insmed"). PARI, Transave, LLC and Insmed shall be referred to collectively as the "Parties."

WHEREAS, pursuant to that certain Agreement and Plan of Merger (the "Merger Agreement"), dated as of December 1, 2010, by and among Insmed, River Acquisition Co., a Delaware corporation and wholly owned subsidiary of Insmed, Transave, LLC, a wholly owned subsidiary of Insmed, Transave, Inc. and the Stockholders' Agent named therein, Transave, Inc. was merged with and into Transave, LLC (the "Merger");

WHEREAS, upon effectiveness of the Merger, the separate corporate existence of Transave, Inc. ceased and, by virtue of the Merger, Transave, LLC, as the surviving company, succeeded to all of the rights, Privileges, powers, franchises, liabilities and obligations of Transave, Inc.;

WHEREAS, the Merger constitutes a Sale of Business Transaction under the Agreement and Transave, LLC and Insmed are successors in interest to Transave, Inc., including for the purposes of Section 5.3(e) of the Agreement;

WHEREAS, the Parties desire that all rights and obligations of Transave, Inc. and Transave, LLC under the License Agreement be assigned to and assumed by Insmed, pursuant to Section 16.4 of the License Agreement; and

WHEREAS the Parties desire to modify the milestones for CF, Bronchiectasis and Non-tuberculosis Mycobacteria infections under the Agreement, all as set forth herein.

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. Capitalized terms used but not defined in this Amendment No. 2 will have the meanings ascribed to them in the Agreement.

2. The CF Milestone Activity and Milestone Deadline chart set forth in Section 7.1(b) of the Agreement is hereby amended as follows (deletions shown as strikethrough and insertions shown in underlining):

Milestone Activity	**Milestone Deadline**
1. **Diligence Milestone 1:** first Phase III Trial for CF begins	[***]
2. **Diligence Milestone 2:** first submission of an MAA application for CF in the Transave Territory	[***]

3. Section 7.1(b)(i) of the Agreement is hereby amended by replacing the date of [***] with [***] and the date of [***] with [***]

4. Section 7.1(b)(ii) of the Agreement is hereby amended by replacing the date of [***] with [***] and the date of [***] with [***]

5. The Bronchiectasis Milestone Activity and Milestone Deadline chart set forth in Section 7.2(a) of the Agreement is hereby amended as follows (deletions shown as strikethrough and insertions shown in underlining):

Milestone Activity	**Milestone Deadline**
1. **Diligence Milestone 1:** Last patient to complete the Phase II Trial for Bronchiectasis	[***]
~~2. **Other Diligence Milestones:** see below~~ 2. **Diligence Milestone 2:** First Phase III Trial for Bronchiectasis begins	[***]
3. **Diligence Milestone 3:** First submission of an MAA application for Bronchiectasis in the Transave Territory	[***]

6. The Non-tuberculosis Mycobacteria Infections Milestone Activity and Milestone Deadline chart set forth in Section 7.2(a) is hereby amended as follows (deletions shown as strikethrough and insertions shown in underlining):

Milestone Activity	**Milestone Deadline**
1. **Diligence Milestone 1:** ~~Last patient to complete the~~ Phase II or III Trial for Non-tuberculosis Mycobacteria infections begins	[***]
2. **Other Diligence Milestones:** see below	

7. Pursuant to Section 16.4 of the Agreement, all rights of Transave, Inc. and Transave, LLC into and under the Agreement, and all obligations and liabilities of Transave, Inc. and Transave, LLC thereunder, are hereby assigned to Insmed, and Insmed hereby accepts such assignment of rights and assumes such obligations and liabilities, and from and alter the date hereof Insmed shall be substituted for Transave Inc. as a party to the License Agreement.

8. The second milestone event and second milestone payment set forth in Section 5.2 of the Agreement is hereby amended as follows (deletions shown as strikethrough and insertions shown in underlining):

2. Initiation of the first Phase III Trial of Drug Product with the Device	[***] [***] **either in cash, Qualified Stock or a combination of cash and Qualified Stock**

9. As partial consideration for this Amendment No. 2, Insmed agrees to pay PARI a fee of [***] immediately upon execution hereof.

10. Upon execution, this Amendment No. 2 shall be made a 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.

[Signatures an Following Page]

IN WITNESS WHEREOF, the Parties have executed this Amendment No. 2 as of the Effective Date indicated above.

INSMED INCORPORATION

By: /s/ Timothy Whitten

Timothy Whitten
President and CEO

Date: 12/22/10

PARI PHARMA GMBH

By: /s/ Martin Knoch

Martin Knoch
President

Date: 01/03/11

TRANSAVE, LLC

By: Insmed Incorporated, Managing Member

By: /s/ Timothy Whitten

Timothy Whitten
President and CEO

Date: 12/22/10

AMENDMENT NO. 3
TO LICENSE AGREEMENT BETWEEN
TRANSAVE, INC. AND PARI PHARMA GMBH

This third amendment ("Amendment No. 3") effective the 6 th day of March, 2012 ("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 and Assignment and Amendment No. 2 the 22 nd day of December 2010 (collectively, the "Agreement"), is entered into between PARI and Insmed Incorporated (successor in interest to Transave, Inc), with registered offices at 9 Deer Park Drive, Suite C, Monmouth Junction, NJ 08852 ("Insmed"). PARI and Insmed shall be referred to collectively as the " **Parties** ."

WHEREAS the Parties desire to modify the milestones for CF, Bronchiectasis and Non-tuberculosis Mycobacteria infections under the Agreement.

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. Capitalized terms used but not defined in this Amendment No. 3 will have the meanings ascribed to them in the Agreement. Where revisions are made, the revisions are to be made to the most recent agreed upon language in effect as of the implementation of the Assignment and Amendment No. 2.

2. The CF Milestone Activity and Milestone Deadline chart set forth in Section 7.1(b) of the Agreement is hereby amended as follows:

Milestone Activity	**Milestone Deadline**
1. **Diligence Milestone 1:** first Phase III Trial for CF begins	[***]
2. **Diligence Milestone 2:** first submission of an MAA application for CF in the Transave Territory	[***]

3. Section 7.1(b)(i) of the Agreement is hereby amended by replacing the date of [***] with [***] and the date of [***] with [***]

4. Section 7.1(b)(ii) of the Agreement is hereby amended by replacing the date of [***] with the date of [***] and the date of [***] with the date of [***]

5. The Bronchiectasis Milestone Activity and Milestone Deadline chart set forth in Section 7.2(a) of the Agreement is hereby amended as:

Milestone Activity	Milestone Deadline
1. **Diligence Milestone 1:** Last patient to complete the Phase II Trial for Bronchiectasis	[***]
2. **Diligence Milestone 2:** First Phase III Trial for Bronchiectasis begins	[***]
3. **Diligence Milestone 3:** First submission of an MAA application for Bronchiectasis in the Transave Territory	[***]

6. The Non-tuberculosis Mycobacteria Infections Milestone Activity and Milestone Deadline chart set forth in Section 7.2(a) is hereby amended as follows:

Milestone Activity	Milestone Deadline
1. **Diligence Milestone 1:** Phase II or III Trial for Non-tuberculosis Mycobacteria infections begins	[***]
2. **Other Diligence Milestones:** see below	

7. In consideration of PARI's agreement to the extensions of the various Milestone Deadlines as set forth above and PARI's continued upholding of exclusivity in the field of Bronchiectasis, Insmed has the option to pay PARI [***]

8. Upon execution, this Amendment No. 3 shall be made a 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. 3 as of the Effective Date indicated above.

INSMED INCORPORATED

By: /s/ Tim Whitten

Tim Whitten
President and CEO

Date: March 8, 2012

PARI PHARMA GMBH

By: /s/ Martin Knoch

Martin Knoch
President

Date: March 6, 2012

AMENDMENT NO. 4
TO LICENSE AGREEMENT BETWEEN
TRANSAVE, INC. AND PARI PHARMA GMBH

This fourth amendment (" **Amendment No. 4** ") effective May 21, 2012 (" **Amendment No. 4 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, and Amendment No. 3 the 6 th day of March 2012 (collectively, the " **Agreement** "), is entered into between PARI and Insmed Incorporated (successor in interest to Transave, Inc.), with registered offices at 9 Deer Park Drive, Suite C, Monmouth Junction, NJ 08852 (" **Insmed** "). PARI and Insmed shall be referred to collectively as the " **Parties** ".

WHEREAS, during the performance of the Agreement, the Parties have made an invention that is directed, in part, to methods of delivering aminoglycosides with a certain nebulization rate, which nebulization rate may be achieved by using the Device of PARI; and

WHEREAS, the Parties now desire to amend the terms and conditions of the Agreement to assign such invention to Insmed such that Insmed will have the sole ownership of such invention.

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. 4 will have the meanings ascribed to them in the Agreement. A new definition is hereby added to the Agreement:

" **Assigned Invention** " means solely the invention described in the invention disclosure attached to Amendment No. 4 as Exhibit A, [***]

2. Assignment of Invention. Notwithstanding anything to the contrary in the Agreement, Insmed shall solely own all right, title and interest in and to the Assigned Invention, which shall be deemed Transave Intellectual Property for purposes of the Agreement and shall be excluded from the definition of Project Intellectual Property. PARI hereby assigns and transfers to Insmed all of its right, title and interest in and to the Assigned Invention free and clear of any encumbrance throughout the world. Upon Insmed's request and at Insmed's cost and expense, PARI shall take, and shall cause its employees and agents to take, all further acts reasonably required to evidence and effect such assignment and transfer to Insmed. For clarity, as the sole owner of Project Data, Insmed shall have the rights, subject to the restrictions set forth in Section 3.2(b) of the Agreement and this Amendment No. 4, to use Project Data in connection with the practice of the Assigned Invention and in support of the filing, prosecution and maintenance of the Assigned Invention Patents (as defined in Paragraph 3 below).

3. Patent Prosecution. As the sole owner of the Assigned Invention, Insmed shall have the sole right and discretion, at its cost and expense, to prepare, file, prosecute and maintain patent applications and patents, including provisionals, additions, divisionals, continuations, substitutions, continuations-in-part, together with re-examinations, reissues, renewals or extensions thereof and all foreign counterparts of the forgoing claiming the Assigned Invention anywhere in the world (the " **Assigned Invention Patent(s)** "), and shall solely own all Assigned Invention Patents. Insmed shall not file or amend any claims in Assigned Invention Patents that [***]. In addition, to the extent that any changes are made that impact or affect PARI Intellectual Property, the Project Intellectual Property or otherwise expand coverage beyond the Transave Field or Non-Compete in Section 4.2 of the Agreement, Insmed shall not file any divisional, continuation, or continuation-in-part of any Assigned Invention Patent without PARI's prior written approval. Upon Insmed's request and at Insmed's cost and expense, PARI shall provide Insmed all reasonable assistance and cooperation in connection with the prosecution and maintenance of the Assigned Invention Patents. Insmed shall keep PARI reasonably informed on the status of Assigned Invention Patents.

4. Joint Ownership of Assigned Invention Patents . Notwithstanding anything to the contrary contained in the Agreement or this Amendment No. 4, if any Assigned Invention Patent contains or is amended to contain any claim that claims, in addition to the Assigned Invention, any embodiment of (i) the Device, (ii) any part of the Device, (iii) any method to manufacture the Device, or (iv) any method of using the Device, then Insmed shall and hereby does transfer and assign to PARI one undivided half interest in such Assigned Invention Patents that include such a claim, so that such Assigned Invention Patents are jointly owned by Insmed and PARI. This Paragraph 4 survives any termination or expiration of the Agreement.

5. PARI Sole Ownership of Assigned Invention Patent(s) . Notwithstanding anything to the contrary contained in the Agreement or this Amendment No. 4, if any Assigned Invention Patent contains or is amended to contain any independent claim that claims any embodiment of (i) the Device, (ii) any part of the Device, (iii) any method to manufacture the Device, or (iv) any method of using the Device, but which does not claim the Assigned Invention, then Insmed shall and hereby does transfer and assign to PARI all right, title and interest in and to the Assigned Invention Patent that contains said independent claim. This Paragraph 5 survives any termination or expiration of the Agreement.

6. License to PARI. Insmed hereby grants to PARI a non-exclusive, perpetual, world-wide, transferable, irrevocable, royalty-free, fully paid-up, sublicenseable license to practice the Assigned Invention and Assigned Invention Patents (the **"Assigned Invention Licenses"**) (i) during the Royalty Term and thereafter outside the Transave Field; and, in addition, (ii) upon early termination of the Agreement by PARI due to Section 15.2 or 15.4, inside the Transave Field to include liposomal aminoglycoside formulations other than Arikace. PARI shall not, and shall not permit any of its Affiliates to, and shall use commercially reasonable efforts to prohibit any of its sublicensees to, (A) practice the Assigned Invention inside the Transave Field, during the Royalty Term, or (B) practice the Assigned Invention in connection with Arikace after earlier termination by PARI under Section 15.2 or 15.4. This Paragraph 5 survives any termination or expiration of the Agreement.

7. Section 1.48 shall hereby be replaced in its entirety as follows:

"Royalty Term" means, on a country-by-country basis, the period commencing on the date of First Commercial Sale of Drug Product and continuing until the later of (a) Expiration of the (i) last Valid Claim covering the particular Device or (ii) the Assigned Invention Patents, in each case in the particular country in which any Product is sold or [***] after the First Commercial Sale of the Drug Product in such country in the Transave Territory.

6. Termination by PARI. Section 15.4 (ii) of the Agreement shall hereby be replaced in its entirety as follows:

[***]

7. Miscellaneous. Upon execution, this Amendment No. 4 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. 4 as of the Amendment No. 4 Effective Date indicated above.

INSMED INCORPORATED	**PARI PHARMA GMBH**
By: /s/ Tim Whitten	By: /s/ Dr. Martin Knoch
Name: Tim Whitten	Name: Dr. Martin Knoch
Title: President and CEO	Title: President
Date: May 12, 2012	Date: May 12, 2012

INSMED -- Confidential Invention Disclosure

[***]

EXHIBIT 21.1

LIST OF SUBSIDIARIES

NAME	JURISDICTION OF INCORPORATION
Insmed Pharmaceuticals, Inc.	Virginia
Celtrix Pharmaceuticals	Delaware
Insmed Limited	England and Wales
Transave, LLC	Delaware

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 No. 333-182124 of Insmed Incorporated, and

(2) Registration Statements on Form S-8 Nos. 333-39200, 333-39198, 333-87878, 333-129479, 333-139744, and 333-175532 of Insmed Incorporated;

of our reports dated March 18, 2013, 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, 2012.

/s/ Ernst & Young LLP

MetroPark, New Jersey
March 18, 2013

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: March 18, 2013

By: /s/ William H. Lewis

William H. Lewis

Chief Executive Officer (Principal Executive Officer) and Director

EXHIBIT 31.2

CERTIFICATION PURSUANT TO

18 U.S.C. 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, 2012 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 U.S.C. § 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

March 18, 2013

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.

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: March 18, 2013

/s/ Andrew T. Drechsler
Andrew T. Drechsler
Chief Financial Officer
(Principal Financial and Accounting Officer)

EXHIBIT 32.2

CERTIFICATION PURSUANT TO

18 U.S.C. 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, 2012 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 U.S.C. § 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)

March 18, 2013

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.