

INSMED INC

FORM 424B5

(Prospectus filed pursuant to Rule 424(b)(5))

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Registration No. 333-218118

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has become effective by rule of the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 5, 2017

PRELIMINARY PROSPECTUS SUPPLEMENT
(To Prospectus dated May 19, 2017)

\$250,000,000



Common Stock

We are offering up to \$250,000,000 of our common stock.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "INSM". The last reported sale price of our common stock on the Nasdaq Global Select Market on September 5, 2017 was \$26.99 per share.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described under the heading "Risk Factors" beginning on page S-8 of this prospectus supplement before buying shares of our common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions ⁽¹⁾	\$	\$
Proceeds, before expenses, to us	\$	\$

⁽¹⁾ We have agreed to reimburse the underwriters for certain expenses in connection with this offering. See "Underwriting".

The underwriters also may purchase up to an additional \$37,500,000 of our common stock at the public offering price, less the underwriting discounts and commissions payable by us, within 30 days from the date of this prospectus supplement. If the underwriters exercise this option in full, the total underwriting discounts and commissions will be \$ _____ and our total proceeds, after underwriting discounts and commissions but before expenses, will be \$ _____.

The underwriters are offering the common stock as set forth under "Underwriting". The underwriters expect to deliver the shares against payment therefor in New York, New York on or about September _____, 2017.

Joint Book-Running Managers

Goldman Sachs & Co. LLC

Leerink Partners

Passive Book-Runner

Evercore ISI

Co-Lead Manager

Stifel

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of common stock and updates the information contained in the accompanying prospectus and the documents incorporated by reference herein and therein. The second part is the accompanying prospectus, which provides more general information, some of which does not apply to this offering. This prospectus supplement and the accompanying prospectus relate to a registration statement that we filed with the U.S. Securities and Exchange Commission ("SEC") using a shelf registration process (File No. 333-218118). To the extent the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus or documents previously filed with the SEC that are incorporated by reference herein, the information in this prospectus supplement will supersede such information. For a more detailed understanding of an investment in our common stock, you should read both this prospectus supplement and the accompanying prospectus, together with the information incorporated by reference herein and therein and additional information described under the heading "Where You Can Find More Information" in the accompanying prospectus.

You should rely only on the information contained or incorporated by reference in this prospectus and the accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. Neither we nor any underwriter has authorized anyone to provide you with information that is different from or in addition to such information. Neither we nor any underwriter is making offers to sell or seeking offers to buy shares of our common stock in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein and any related free writing prospectus is accurate only as of the respective dates of such documents, regardless of the time of delivery of this prospectus supplement or any sale of the common stock offered hereby. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus supplement and the accompanying prospectus to "Insmmed", the "Company", "we", "us" and "our" refer to Insmmed Incorporated, a Virginia corporation, together with its consolidated subsidiaries. INSMED and ARIKAYCE are trademarks of Insmmed Incorporated. Our logos and trademarks are the property of Insmmed. All other brand names or trademarks appearing in this prospectus supplement and the accompanying prospectus are the property of their respective holders. Use or display by us of other parties' trademarks or trade dress in this prospectus supplement and the accompanying prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the other documents that are incorporated herein by reference contain forward-looking statements that involve substantial risks and uncertainties. "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 such as "may", "will", "should", "could", "would", "expects", "plans", "anticipates", "believes", "estimates", "projects", "predicts", "intends", "potential", "continues", and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) identify forward looking statements.

Forward looking statements are based on our current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause our actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timing discussed, projected, anticipated or indicated in any forward looking statements. Such risks, uncertainties and other factors include, among others, the following:

- risks that the full six-month data from the CONVERT study (the "CONVERT study" or the "212 study") or subsequent data from the remainder of the study's treatment and off-treatment phases will not be consistent with the top-line six-month results of the study;
- uncertainties in the research and development of our existing product candidates, including due to delays in data readouts, such as the full data from the CONVERT study, patient enrollment and retention or failure of our preclinical studies or clinical trials to satisfy pre-established endpoints, including secondary endpoints in the CONVERT study and endpoints in the CONVERT extension study (the "312 study");
- failure to obtain, or delays in obtaining, regulatory approval from the U.S. Food and Drug Administration ("FDA"), Japan's Ministry of Health, Labour and Welfare ("MHLW"), the European Medicines Agency ("EMA"), and other regulatory authorities for our product candidates or their delivery devices, such as the eFlow Nebulizer System, including due to insufficient clinical data, selection of endpoints that are not satisfactory to regulators, complexity in the review process for combination products or inadequate or delayed data from a human factors study required for U.S. regulatory approval;
- failure to maintain regulatory approval for our product candidates, if received, due to a failure to satisfy post-approval regulatory requirements, such as the submission of sufficient data from confirmatory clinical studies;
- safety and efficacy concerns related to our product candidates;
- lack of experience in conducting and managing preclinical development activities and clinical trials necessary for regulatory approval, including the regulatory filing and review process;
- failure to comply with extensive post-approval regulatory requirements or imposition of significant post-approval restrictions on our product candidates by regulators;
- uncertainties in the rate and degree of market acceptance of product candidates, if approved;
- inability to create an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of our product candidates, if approved;
- inaccuracies in our estimates of the size of the potential markets for our product candidates or limitations by regulators on the proposed treatment population for our product candidates;

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- failure of third parties on which we are dependent to conduct our clinical trials, to manufacture sufficient quantities of our product candidates for clinical or commercial needs, including our raw materials suppliers, or to comply with our agreements or laws and regulations that impact our business;
- inaccurate estimates regarding our future capital requirements, including those necessary to fund our ongoing clinical development, regulatory and commercialization efforts as well as milestone payments or royalties owed to third parties;
- failure to develop, or to license for development, additional product candidates, including a failure to attract experienced third-party collaborators;
- uncertainties in the timing, scope and rate of reimbursement for our product candidates;
- changes in laws and regulations applicable to our business and failure to comply with such laws and regulations;
- inability to repay our existing indebtedness or to obtain additional capital when needed;
- failure to obtain, protect and enforce our patents and other intellectual property and costs associated with litigation or other proceedings related to such matters;
- restrictions imposed on us by license agreements that are critical for our product development, including our license agreements with PARI Pharma GmbH ("PARI") and AstraZeneca AB ("AstraZeneca"), and failure to comply with our obligations under such agreements;
- competitive developments affecting our product candidates and potential exclusivity related thereto;
- the cost and potential reputational damage resulting from litigation to which we are a party, including, without limitation, the class action lawsuit pending against us;
- loss of key personnel;
- lack of experience operating internationally; and
- risks that the net proceeds from the offering are not spent as currently intended or in ways that enhance the value of your investment in our common stock.

We may not actually achieve the results, plans, intentions or expectations indicated by our forward-looking statements because, by their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future. These risks and uncertainties include, but are not limited to, those described in the "Risk Factors" section of this prospectus supplement.

We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they were made. We disclaim any obligation, except as specifically required by law, and the rules of the SEC, 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 such forward-looking statements.

You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein with the understanding that our actual future results may be materially different from those expressed in forward-looking statements.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information included or incorporated by reference in this prospectus supplement and the accompanying prospectus and does not contain all of the information that may be important to you. You should carefully review this entire prospectus supplement and the accompanying prospectus, including the risk factors and financial statements and related notes thereto included and incorporated by reference herein and therein, before making an investment decision to purchase our common stock.

Overview

Insmed is a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. Our lead product candidate is amikacin liposome inhalation suspension ("ALIS") (formerly known as liposomal amikacin for inhalation), which is in late-stage development for adult patients with treatment refractory nontuberculous mycobacteria ("NTM") lung disease caused by *Mycobacterium avium* complex ("MAC"), a rare and often chronic infection that can cause irreversible lung damage and which can be fatal. Our earlier clinical-stage pipeline includes INS1007 and INS1009. INS1007 is a novel oral, reversible inhibitor of dipeptidyl peptidase 1, an enzyme responsible for activating neutrophil serine proteases, which are implicated in the pathology of chronic inflammatory lung diseases, such as non-cystic fibrosis ("non-CF") bronchiectasis. INS1009 is an inhaled nanoparticle formulation of a treprostinil prodrug that may offer a differentiated product profile for rare pulmonary disorders, including pulmonary arterial hypertension ("PAH").

Recent Developments

Top-Line Efficacy Data

We recently announced top-line data for the CONVERT study, which enrolled 336 adult patients with NTM lung disease caused by MAC who were refractory to at least six months of treatment on current guidelines-based therapy ("GBT"). After a screening period of up to 10 weeks, eligible patients were randomized 2:1 to once-daily ALIS plus GBT or GBT only. The primary endpoint of the study was the proportion of patients achieving culture conversion, which we defined as three consecutive monthly negative sputum cultures, by month 6. Based on top-line results, the CONVERT study met its primary endpoint, with 29% of patients in the ALIS plus GBT arm achieving culture conversion, compared to 9% of patients in the GBT-only arm ($p < 0.0001$).

We also reported top-line data for certain secondary and exploratory endpoints for the first six months of the study. Top-line data for the six-minute walk test indicated no statistically significant difference between patients in the two arms of the study. However, an analysis of these data (per a pre-specified exploratory endpoint) showed that patients who achieved culture conversion in either arm demonstrated an improvement in six-minute walk distance when compared to patients who did not culture convert ($p = 0.0108$). Top-line data for the secondary endpoint of time to conversion demonstrated that patients in the GBT-only arm took approximately 30% longer to convert when compared to patients on ALIS plus GBT ($p < 0.0001$). We are continuing our analysis of the impact of conversion on a variety of other clinical measures.

We plan to pursue accelerated approval of ALIS pursuant to 21 C.F.R. Part 314 Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) ("Subpart H") based on the data from the CONVERT study.

Top-Line Safety and Tolerability Data

Approximately 98 percent of patients in the ALIS plus GBT arm of the study experienced at least one treatment-emergent adverse event ("TEAE"), compared to 91 percent of patients in the GBT-only arm, with most events being mild or moderate in severity. A greater percentage of patients in the ALIS plus GBT arm than in the GBT-only arm experienced TEAEs involving dysphonia, cough, haemoptysis, dyspnoea, oropharyngeal pain, diarrhoea, nausea, and fatigue. Based on our review of the top-line study safety data, the incidence of dysphonia, cough and dyspnoea among patients in the ALIS plus GBT arm generally decreased after the second study month. Approximately 20 percent and 18 percent of patients in the ALIS plus GBT arm and GBT-only arm of the study respectively experienced at least one serious treatment emergent adverse event ("STEAE"). The table below provides additional information regarding certain STEAEs experienced by patients in the study.

Patients Reporting STEAEs >3% in Either Arm		2:1 Randomization	
		ALIS + GBT (n=223)	GBT (n=112)
Patients Reporting At Least One STEAE		20.2% (45)	17.9% (20)
System Organ Class	Preferred Term		
Respiratory, Thoracic, Mediastinal Disorders		11.7% (26)	9.8% (11)
	Hemoptysis	2.7% (6)	4.5% (5)
	COPD (exacerbation)	3.1% (7)	0.9% (1)
Infections and Infestations		9.0% (20)	5.4% (6)
	Pneumonia	3.6% (8)	1.8% (2)
Cardiac Disorders		0.4% (1)	4.5% (5)
Patient Deaths		2.7% (6)	4.5% (5)

There were no distinctions between treatment arms for adverse events of hearing loss or renal impairment, side effects commonly associated with the intravenous use of amikacin. The overall dropout rate was 16.1 percent, with an 8.9 percent dropout rate in the GBT-only arm and a 19.6 percent rate in the ALIS plus GBT arm.

Market Opportunity for ALIS in NTM Lung Disease in 2018

NTM lung disease is associated with increased rates of morbidity and mortality, and MAC is the predominant pathogenic species in NTM lung disease in the United States, Japan and Europe. The prevalence of NTM lung disease has increased over the past two decades, and we believe it is an emerging public health concern worldwide. Based on currently available information from external sources, including market research funded by us and third parties, and internal analyses and calculations, we estimate potential patient populations in the United States, Japan and EU5 (comprised of France, Germany, Italy, Spain and the United Kingdom) for 2018 as follows:

Potential Market	Estimated Number of Patients with Diagnosed NTM Lung Disease	Estimated Number of Patients Treated for NTM Lung Disease Caused by MAC	Estimated Number of Patients Refractory to Treatment
United States	75,000 – 105,000	40,000 to 50,000	10,000 – 15,000
Japan	125,000 – 145,000	60,000 – 70,000	15,000 – 18,000
EU5	14,000	4,400	1,400

See "Forward-Looking Statements" and "Risk Factors" beginning on pages S-2 and S-8 of this prospectus supplement for further information regarding the assumptions made in developing these estimates and the factors that may cause them to differ materially from actual patient populations in these markets.

We are not aware of any approved inhaled therapies specifically indicated for NTM lung disease in North America, Japan or Europe. Current guideline-based approaches for NTM lung disease, including those from the American Thoracic Society and Infectious Diseases Society of America, involve multi-drug regimens not approved for the treatment of NTM lung disease and treatment that could last two years or more. Based on a burden of illness study that we conducted in the United States with a major medical benefits provider, we previously concluded that patients with NTM lung disease are costly to healthcare plans, while a recent claims-based study in the United States has shown that patients with NTM lung disease have higher resource utilization and costs than their age and gender-matched controls. Accordingly, we believe that a significant market opportunity for ALIS in NTM lung disease exists in the United States and internationally.

Corporate Information

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 company focused on the development of differentiated and innovative inhaled pharmaceuticals for the site specific treatment of serious lung diseases ("Transave"). Our principal executive offices are located at 10 Finderne Avenue, Building 10, Bridgewater, NJ 08807, and our telephone number is (908) 977-9900. Our website address is www.insmed.com. The information on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus and should not be considered to be part of either document.

THE OFFERING

Common stock offered by us	shares.
Common stock to be outstanding after this offering	shares or shares if the underwriter's option to purchase additional shares is exercised in full.
Use of proceeds	We intend to use the net proceeds from this offering to fund ongoing and future clinical development of ALIS for patients with NTM lung disease caused by MAC and our efforts to obtain potential regulatory approvals for and, if approved, commercialize ALIS in its approved indication; invest in increased third-party manufacturing capacity for and commercial inventory production of ALIS in anticipation of possible commercial launch, initially in the United States and subsequently in Japan and other countries; fund further clinical development of INS1007; and fund working capital, potential debt repayment, capital expenditures, general research and development; and for other general corporate purposes, which may include the acquisition or in-license of additional compounds, product candidates, technology or businesses. See "Use of Proceeds" on page S-38 of this prospectus supplement for additional information.
Risk Factors	An investment in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-8 of this prospectus supplement before deciding to invest in shares of our common stock.
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to additional shares of our common stock.
Nasdaq Global Select Market listing	Our common stock is listed on the Nasdaq Global Select Market under the symbol "INSM".

The number of shares of our common stock to be outstanding immediately after this offering is based on 62,376,416 shares of our common stock outstanding as of June 30, 2017.

The number of shares of our common stock to be outstanding immediately after this offering excludes:

- 8,621,451 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2017 at a weighted average exercise price of \$13.87 per share;
- 46,914 shares of our common stock issuable pursuant to unvested restricted stock units outstanding as of June 30, 2017 at a weighted average grant price of \$17.16; and
- 4,978,554 shares of our common stock reserved for issuance under our 2017 Incentive Plan as of June 30, 2017, plus any shares subject to outstanding awards as of May 18, 2017 under our 2015 Incentive Plan and 2013 Incentive Plan that subsequently are cancelled, terminated unearned, expired, forfeited, lapsed for any reason or are settled in cash without the delivery of shares.

Unless otherwise stated, all information in this prospectus supplement excludes the shares referenced in the bullets immediately above and assumes no exercise by the underwriters of their option to purchase additional shares.

RISK FACTORS

An investment in our common stock involves significant risks. Before making an investment in our common stock, you should carefully read all of the information contained in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein. For a discussion of risks that you should carefully consider before deciding to purchase any of our common stock, please review the risk factors disclosed below, together with the other information in this prospectus supplement, the accompanying prospectus, and the information and documents incorporated by reference herein and therein. Any of these risks, as well as additional risks not currently known to us or that we currently deem immaterial, may adversely affect our business, financial condition, results of operations, and prospects, resulting in a decline in the trading price of our common stock and loss of all or part of your investment.

Risks Related to Development, Regulatory Approval and Commercialization of our Product Candidates

The currently reported results of the CONVERT study are based on top-line data for the first six months of the study and may differ from complete study results once additional data are received and evaluated.

The reported results of our CONVERT study, which are discussed herein, consist of only top-line data from the first six months of the study. Top-line data are based on a preliminary analysis of currently available efficacy and safety data, and therefore these currently reported results are subject to change following a comprehensive review of the more extensive data we expect to receive for patients as of month six. Top-line data are based on important assumptions, estimations, calculations and information currently available to us, and we have not received or had an opportunity to evaluate all of the six-month data from the CONVERT study. As a result, the top-line six-month results may differ from the full six-month data, or different conclusions or considerations may qualify such top-line results, once the complete six-month data have been received and fully evaluated. In addition, the CONVERT study is ongoing, and subsequent data from the treatment and off-treatment phases of the study may differ from the currently reported top-line results. If these top-line data differ from the results of the full six-month data or subsequent data from patients during the remainder of the treatment phase or the off-treatment phase, our ability to obtain or maintain approval for, and commercialize, ALIS may be harmed, which could materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Our prospects are highly dependent on the success of our most advanced product candidate, ALIS. If we are unable to successfully complete the development of, obtain or subsequently maintain regulatory approval for, and successfully commercialize ALIS, our business, financial condition, results of operations and prospects and the value of our common stock will be materially adversely affected.

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

Positive results from preclinical studies of a product candidate may not be predictive of similar results in human clinical trials, and promising results from earlier clinical trials of a product 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, even if the full six-month

data for the primary endpoint are positive, such data may not be predictive of the results from the remainder of the study or the 312 study, or future trials related to ALIS.

In addition, even if we believe our clinical trials for ALIS demonstrate promising results, regulators may decline to grant regulatory approval. For instance, in the fourth quarter of 2014, we filed a marketing authorization application ("MAA") with the EMA for ALIS as a treatment for, among other things, NTM lung disease in adult patients. The filing was based in part on data from our phase 2 study in patients with NTM lung disease. In addition, we subsequently withdrew our MAA after the Committee for Medicinal Products for Human Use ("CHMP") concluded that the data submitted did not provide enough evidence to support an approval. We currently expect to submit a new drug application ("NDA") to the FDA pursuant to Subpart H for ALIS based on the efficacy data from the CONVERT study through month 6. Although we view the top-line six-month results from the CONVERT trial as promising, the FDA may not agree that this data is sufficient to support submission or approval of our NDA under Subpart H.

Further, even if we obtain approval for ALIS from a regulator, including from the FDA pursuant to Subpart H, such approval may be withdrawn under certain circumstances and confirmatory clinical studies may be required and could fail to demonstrate sufficient safety and efficacy to support continued approval. For instance, if we obtain approval from the FDA based on the NDA filing described above, the FDA may nonetheless conclude that the data generated from the remainder of the CONVERT study or in the 312 study is not sufficient to support continued approval of our NDA.

We do not expect ALIS to be commercially available in any market until we receive requisite approval from the FDA, MHLW, EMA or an equivalent regulatory agency. The failure to obtain or subsequently maintain such approvals will materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

We may not be able to obtain regulatory approvals for ALIS or any other products we develop in the U.S., Japan, Europe or other markets. 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, and the failure to do so will prevent us from commercializing our products, which would materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock. The regulatory review and approval processes in the U.S., Japan and Europe require evaluation of preclinical studies and clinical studies, as well as the evaluation of our manufacturing process. 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. These processes are complex, lengthy, expensive, resource intensive and uncertain. We have limited experience in submitting and pursuing applications necessary to gain these regulatory approvals.

As described above, data submitted to regulators is subject to varying interpretations that could delay, limit or prevent regulatory agency approval. We may also encounter delays or rejections based on changes in regulatory agency policies during the period in which we develop a product and the period required for review of any application for regulatory agency approval of a particular product. For example, the FDA has designated ALIS for fast track, breakthrough therapy and qualified infectious disease product status, all programs intended to expedite or streamline the development and regulatory review of the drug. If we were to lose the current designation under one or more of those programs, we could face delays in the FDA review and approval process. 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 and prospects and the value of our common stock. Even with these designations, there is no guarantee we will receive approval for ALIS on a timely basis, or at all.

Similarly, we are currently assessing our regulatory strategies with regard to orphan drug designation and other pathways that could expedite the development and regulatory review of INS1007 in the U.S. and the EU, but we may be unsuccessful in pursuing such strategies. The FDA recently denied our initial request for orphan drug designation for INS1007 in non-CF bronchiectasis, and we are evaluating our options, including whether to appeal this decision or reapply for this designation based on a refined regulatory strategy. In addition, although we believe that INS1009 could be eligible for approval under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act ("505(b)(2)"), and thus could rely at least in part on studies not conducted by or for us and for which we do not have a right of reference, we may not obtain approval from the FDA to use this pathway.

Approval by the FDA does not ensure approval by the regulatory authorities of other countries. To market our products outside of the U.S., we, and potentially our third-party providers, 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 approval. In addition, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions (including with respect to our target market) and criminal prosecution if we fail to comply with applicable U.S. or foreign regulatory requirements.

We have not completed the research and development stage of ALIS or any other product candidates. If we are unable to successfully develop and commercialize ALIS or any other products, it will materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Our long-term viability and growth depend on the successful commercialization of ALIS and potentially other product candidates. 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 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 practices and good clinical practices and disease-specific expectations of the FDA and other regulatory bodies;
- Select and recruit clinical investigators and subjects for our studies;
- Collect, analyze and correctly interpret the data from our studies;
- Obtain data establishing adequate safety of our product candidates and demonstrating with statistical significance that our product candidates are effective for their proposed indications, as indicated by satisfaction of pre-established endpoints;
- Submit for and receive regulatory approvals for marketing;
- Submit for and receive reimbursement approvals for market access; and

- Manufacture the product candidates and device components according to current good manufacturing practices ("CGMP").

The development program with respect to any given product will take many years and thus delay our ability to generate profits associated with that product. 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, or regulators may require additional testing to substantiate our claims. For instance, as described above, although we view the top-line six-month results from the CONVERT study as promising, our clinical studies of ALIS for refractory NTM lung disease caused by MAC are ongoing, and outcomes from those studies cannot be predicted. If we do not proceed with the development of our ALIS program in the NTM lung disease or cystic fibrosis ("CF") indications, certain of our contract counterparties may elect to proceed with the development of these indications. Even if we are successful in obtaining regulatory approval for our product candidates, including ALIS, we may not obtain labeling that permits us to market them with commercially viable claims because the final wording of the approved indication may be restrictive, or the available clinical data may not provide adequate comparative data with other products. Failure to successfully commercialize our products will materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

If our clinical studies do not produce positive results or our clinical trials are delayed, or if serious side effects are identified during drug development, we may experience delays, incur additional costs and ultimately be unable to commercialize our product candidates in the U.S., Japan, Europe or other markets.

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.

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

- Our preclinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical testing or clinical trials or we may abandon projects that we expect to be promising;
- Regulators, ethics committees or institutional review boards ("IRBs") 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 experience difficulties or delays due to the number of clinical sites involved in our clinical trials;
- We may decide to limit or abandon our commercial development programs;

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- Conditions imposed on us by the FDA or any non-U.S. regulatory authority regarding the scope or design of our clinical trials may require us to collect and submit information to regulatory authorities, ethics committees, IRBs 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 ("CROs"), clinical investigators, clinical laboratories, product suppliers or nebulizer supplier may fail to comply with regulatory requirements or fail to meet their contractual obligations to us in a timely manner;
- We may have to suspend or terminate one or more of our clinical trials if we, regulators, ethics committees or the IRBs 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, ethics committees or IRBs 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;
- 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; and
- Our competitors may be able to bring products to market before we do.

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:

- Experience increased product development costs, as we have in the past;
- Be delayed in obtaining, or be unable to obtain, regulatory 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 labeling with black box or other warnings or contraindications;
- Have the product removed from the market after obtaining regulatory approval; or
- Face a shortened patent protection period during which we may have the exclusive right to commercialize 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, MHLW, EMA and other regulatory agencies.

We have limited experience in conducting and managing the preclinical development activities and clinical trials necessary to obtain regulatory approvals, including approval by the FDA, MHLW and EMA, which might prevent us from successfully designing, implementing, or completing the clinical trials required to support regulatory approval of our product candidates. Since our merger with Transave, we have not completed a regulatory filing and review process for, obtained regulatory approval of or commercialized any of our product candidates. The application processes for the FDA, MHLW, Pharmaceutical and Medical Devices Agency, EMA and other regulatory agencies are complex and difficult and vary by regulatory agency, and we have limited experience in conducting and managing the application processes necessary to obtain regulatory approvals in these various jurisdictions and 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 ALIS or other product candidates, or might be significantly delayed in doing so, which may materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

There is little or no precedent for clinical development and regulatory expectations for agents to treat NTM lung disease; as a result, we may encounter challenges developing clinical endpoints that will ultimately be satisfactory to regulators, which could cause our product candidates not to be approved by regulators, delay commercialization of our product candidates or subject us to the risk of having any approval withdrawn.

Based on the top-line six-month data from the CONVERT study, we expect to submit an NDA under Subpart H to request accelerated approval for ALIS. The FDA may base accelerated approval for drugs intended to treat serious or life-threatening illnesses that provide meaningful therapeutic benefit to patients over existing treatments on whether the drug has an effect on a surrogate or an intermediate clinical endpoint (other than survival or irreversible morbidity). We are using a surrogate endpoint in our CONVERT study and, while we have discussed our protocol for potential accelerated approval under Subpart H with the FDA, the FDA has not indicated its agreement or disagreement with the protocol. In addition, the FDA has indicated that the results of the six-minute walk test, a secondary endpoint in the CONVERT study, will be important in assessing the results of culture conversion as a surrogate endpoint in the CONVERT study. Developing clinical endpoints that are unsatisfactory to regulators could delay clinical trials and the FDA approval process, which could materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Additionally, if ALIS or any of our other product candidates is approved based on a surrogate or an intermediate clinical endpoint under the accelerated approval regulations, the approval will be subject to the requirement that we study the product candidate further to verify and describe its clinical benefit, where there is uncertainty as to the relation of the surrogate or intermediate clinical endpoint to clinical benefit or of the observed clinical benefit to the ultimate outcome. Thus, even if we are successful in obtaining accelerated approval in the U.S. or under comparable pathways in other jurisdictions, we may face requirements and limitations that will adversely affect our prospects. For example, we may be approved only for a very limited indication, we may not successfully complete required post-approval trials, or such trials may not confirm the clinical benefit of our drug, and approval of the drug may be withdrawn.

For ALIS to be successfully developed and commercialized in a given market, in addition to regulatory approvals required for ALIS, the eFlow Nebulizer System must satisfy certain regulatory requirements and its use as a delivery system for ALIS must be approved or cleared by regulators.

ALIS is administered using the eFlow Nebulizer System. As such, the eFlow Nebulizer System must receive regulatory approval or clearance on its own or in conjunction with ALIS as a combination product in order for us to develop and commercialize ALIS. Although the eFlow Nebulizer System is CE marked by PARI in the EU, outside the EU, it is labeled as investigational for use in our clinical trials, including in the U.S., Japan, Canada and Australia. The eFlow Nebulizer System is not approved for commercial use in the U.S., Japan, Canada or certain other markets in which we may seek to commercialize ALIS.

In the U.S., we plan to seek approval of the eFlow Nebulizer System in conjunction with ALIS as a combination product through a single NDA submission, and the increased complexity of the review process in this circumstance may delay approval. Additionally, while we continue to work closely with PARI to coordinate efforts regarding regulatory requirements, we will be responsible for this NDA submission, and we, in consultation with PARI, may not be successful in meeting the regulatory requirements for the eFlow Nebulizer System, which would prevent or delay our ability to bring ALIS to market or to market it successfully. Further, based on our discussions to date with the FDA, we will need to conduct a human factors study for the eFlow Nebulizer System prior to submission of our NDA for ALIS. Preparations for this study are underway, but if the study is delayed or otherwise does not yield adequate data, it could prevent or delay submission of the NDA or approval of ALIS.

We may not be able to enroll enough patients to complete our clinical trials or retain a sufficient number of patients in our clinical trials to generate the data necessary for regulatory approval of our product candidates.

The completion rate of our clinical studies 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;
- Discontinuation rates; and
- Competition from other companies' potential clinical studies for the same patient population.

Delays in patient enrollment for future clinical trials, such as those we encountered in enrolling the CONVERT study, could increase costs and delay ultimate commercialization and sales, if any, of our products. Once enrolled, patients may elect to discontinue participation in a clinical trial at any time. If patients elect to discontinue participation in our clinical trials at a higher rate than expected, we may be unable to generate the data required by regulators for approval of our product candidates.

Even if we obtain regulatory approval for ALIS 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 regulatory approval in the U.S. is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing, including risk evaluation and mitigation strategies ("REMS"), 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 postmarket information;
- Monitoring and reporting complaints, adverse events and instances of the failure of a product to meet specifications;
- Compliance with CGMPs;
- 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 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 of 1987;
- Sales, marketing and scientific or educational grant programs must comply with federal and state laws; and
- Pricing and rebate programs must comply with the Medicaid rebate requirements, 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.

If we 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 regulatory approval;
- Suspend or terminate 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; and/or
- 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.

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

Even if we are able to successfully complete development of, obtain regulatory approval for, and bring to market our product candidates, they may not gain market acceptance by physicians, patients, third-party payers and others in the medical community. If ALIS, or any other product candidate we bring to market, does 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 ALIS 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 products;
- Relative convenience and ease of administration;
- The willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- The strength of marketing and distribution support and timing of market introduction of competitive products;
- Publicity concerning our products or competing products and treatments, including competing products becoming subject to generic pricing; and
- Sufficient third-party insurance coverage and reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical and clinical trials, market acceptance of the product will not be known until after it is launched. For example, if a clinical trial is not designed to demonstrate advantages over alternative treatments, we may be prohibited from promoting our product candidates on any such advantages. Our efforts to educate the medical community and third-party payers on the benefits of our product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required to commercialize more established technologies marketed by our competitors.

We currently have a very small marketing and 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, our ability to generate product revenues will be adversely affected.

We have a small commercial organization for the marketing, market access, sales and distribution of our products. In order to commercialize ALIS 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 will be expensive and time consuming and could delay any product launch, and we may be unable 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 ALIS in certain markets. However, we may not be able to enter into arrangements with third parties to sell ALIS on favorable terms or at all. In the event we are unable to develop our own marketing, market access, and sales force or collaborate with a third-party marketing, market access, and sales organization, we may not be able to successfully commercialize ALIS 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.

If estimates of the size of the potential markets for our product candidates, including ALIS, are overstated or regulators limit the proposed treatment population for our product candidates, our ability to commercialize such product candidates successfully or achieve sufficient revenue to support our business could be materially adversely affected.

We have relied on currently available information from external sources, including market research funded by us and third parties, and internal analyses and calculations to estimate the potential market opportunities for NTM lung disease in 2018 in the United States, Japan and EU5. The externally sourced information used to develop these estimates has been obtained from sources we believe to be reliable, but we have not verified the data from such sources, and their accuracy and completeness cannot be assured. Similarly, our internal analyses and calculations are based upon management's understanding and assessment of numerous inputs and market conditions, including, but not limited to, the projected increase in prevalence of NTM lung disease, Medicare patient population growth and ongoing population shifts to geographies with increased rates of NTM lung disease. These understandings and assessments necessarily require assumptions subject to significant judgment and may prove to be inaccurate. As a result, our estimates of the size of these potential markets for ALIS could prove to be overstated, perhaps materially. We may develop estimates with respect to market opportunities for other product candidates in the future, and such estimates would be subject to similar risks. In addition, a potential market opportunity could be reduced if a regulator limits the proposed treatment population for one of our product candidates. In either circumstance, even if we obtain regulatory approval for a product candidate, we may be unable to commercialize it on a scale sufficient to generate material revenues, which could have a material adverse effect on our business, financial condition, results of operations and prospects and the value of our common stock.

Risks Related to Our Reliance on Third Parties

We rely on third parties including collaborators, CROs, clinical and analytical laboratories, contract manufacturing organizations ("CMOs") and other providers for many services that are critical to our business. If we are unable to form and sustain these relationships, or if any third-party arrangements that we may enter into are unsuccessful, including due to non-compliance by such third parties with our agreements or applicable law, our ability to develop and commercialize our products may be materially adversely affected.

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

- Significant competition in seeking appropriate partners;
- The complex and time-consuming nature of negotiation, documentation and implementation of agreements with third parties in the pharmaceutical industry;

- Our potential inability to establish and implement collaborations or other alternative arrangements that we might pursue on favorable terms;
- Our potential inability to control whether third parties devote sufficient resources to our programs or products, including with respect to meeting contractual deadlines;
- Our potential inability to control the regulatory and contractual compliance of third parties, including their processes and procedures, systems utilized to collect and analyze data, and equipment used to test drug product and/or clinical supplies;
- Disagreements with third parties, including CROs, that result in a dispute over and loss of intellectual property rights, delay or termination of research, development, or commercialization of product candidates or litigation or arbitration;
- Contracts with our collaborators that fail to provide sufficient protection of our intellectual property; and
- Difficulty enforcing the contracts if one of these third parties fails to perform.

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

Such risks could materially harm our business, financial condition, results of operations and prospects and the value of our common stock.

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, which would materially harm our business.

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. For instance, we are and expect to remain dependent upon Therapure Biopharma Inc. ("Therapure"), Ajinomoto Althea, Inc. ("Althea") and other suppliers being able to provide an adequate supply of ALIS both for our clinical trials and for commercial sale in the event ALIS receives regulatory approvals. Althea currently manufactures ALIS at a relatively small scale. In order to meet potential commercial demand, if ALIS is approved, we have constructed a manufacturing operation at Therapure in Canada that operates at a larger scale and intend to invest in additional production capacity for ALIS. We may not be able to secure such additional production capacity for ALIS, which would increase the risks associated with either Therapure or Althea being unable to provide us with an adequate supply of ALIS.

We are also dependent upon PARI being able to provide an adequate supply of nebulizers both for our clinical trials and for commercial sale in the event ALIS receives regulatory approval, as

PARI is the sole manufacturer of the eFlow Nebulizer System. We have no alternative supplier for the nebulizer, and we do not intend to seek an alternative or secondary supplier. Significant effort and time were expended in the optimization of the nebulizer for use with ALIS. In the event PARI cannot provide us with sufficient quantities of the nebulizer, replication of the optimized device by another party may require considerable time and additional regulatory approval. In the case of certain defined supply failures, we will have the right under the our commercialization agreement with PARI to make the nebulizer and have it made by certain third parties, but not those deemed under the commercialization agreement to compete with PARI.

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. In such circumstances, an inadequate supply of ALIS or the nebulizer could delay, impair or prevent clinical trials, the development and commercialization of ALIS and adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Risks Related to Our Financial Condition and Future Capital Requirements

We have a history of operating losses, and we currently have no material source of revenue. We expect to incur operating losses for the foreseeable future and may never achieve or maintain profitability.

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, and we did not generate material revenue during the six months ended June 30, 2017 or the years ended December 31, 2016, 2015 or 2014. 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 product candidates would require us to significantly expand our sales and marketing organization and establish contractual relationships to enable product manufacturing and other related activities. We expect that our activities, together with our general and administrative expenses, will continue to result in substantial operating losses for the foreseeable future. As of June 30, 2017, our accumulated deficit was \$847.3 million. For the six months ended June 30, 2017, our consolidated net loss was \$82.1 million, and we incurred a consolidated net loss of \$176.3 million for the year ended December 31, 2016. To achieve and maintain profitability, we need to generate significant revenues from future product sales. The process of developing and commercializing our products will require significant expenditures for pre-clinical and clinical testing, regulatory approvals for commercialization and marketing, development of an internal or external sales and marketing organization and other related activities. Because of the numerous risks and uncertainties associated with drug development and commercialization, we are unable to predict the extent of any future losses, and we may never generate significant future revenues or achieve and sustain profitability.

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 ALIS. In addition, if we obtain regulatory approval for ALIS or any of our other product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We will need additional capital to fund these expenses. We also will require additional future capital in order to continue our other research

and development activities, including due to changes in our product development plans or misjudgment of expected costs, fund corporate development, maintain our intellectual property portfolio or resolve litigation. As of June 30, 2017, we had \$91.1 million of cash and cash equivalents on hand but no committed sources of capital. We do not know whether additional financing will be available when needed, or, if available, that the terms will be favorable. If adequate funds are not available to us when needed, we will be forced to delay, restrict or eliminate all or a portion of our development programs or commercialization efforts.

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

Our loan agreement with Hercules, under which we had outstanding indebtedness of \$55.2 million as of June 30, 2017, 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 shareholders. The loan agreement also contains certain other covenants (including limitations on other indebtedness, liens, acquisitions, investments and dividends). 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 Hercules 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, Hercules has the right to participate, in an amount of up to \$2.0 million, in a subsequent private financing that involves the issuance of our equity securities. The interest-only period under the loan agreement extends through November 1, 2018, and can be extended up to six months under certain conditions. The maturity date of the loan facility is October 1, 2020.

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, Hercules may have the right to seize the assets securing our obligations under the loan agreement. The terms and restrictions provided in the loan agreement may inhibit our ability to conduct our business and to maximize shareholder value. Future debt securities or other financing arrangements could contain negative covenants similar to, or even more restrictive than, the Hercules loan agreement.

In-process research and development ("IPRD") comprised approximately 35% of our total assets as of June 30, 2017. A reduction in the value of our IPRD could have a material adverse effect on our results of operations, financial condition and the value of our common stock.

As a result of the merger with Transave in 2010, we recorded an intangible IPRD asset of \$77.9 million and goodwill of \$6.3 million on our balance sheet. As a result of the clinical hold on ALIS announced in late 2011, we recorded a charge of \$26.0 million in the fourth quarter of 2011 that reduced the value of IPRD to \$58.2 million and reduced goodwill to zero. Potential future activities or results could result in additional writedowns of IPRD, which could materially adversely affect our results of operations, financial condition and the value of our common stock.

We may be unable to use our net operating losses and other tax assets.

We have substantial tax loss carry forwards for U.S. federal income tax and state income tax purposes, and beginning in 2015, we had tax loss carry forwards in Ireland as well. In general, our net operating losses and tax credits have been fully offset by a valuation allowance due to uncertainties surrounding our ability to realize these tax benefits. In particular, our ability to fully use certain U.S. tax loss carry forwards and general business tax credit carry forwards recorded prior to December 2010 to offset future income or tax liability is limited under section 382 of the Internal Revenue Code of 1986, as amended (the "Code"). Changes in the ownership of our stock, including those resulting from the issuance of shares of our common stock in this or future offerings or upon exercise of outstanding options, may limit or eliminate our ability to use certain net operating losses and tax credit carry forwards in the future.

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

As part of our business strategy, we may effect acquisitions to obtain additional businesses, products, technologies, capabilities and personnel, but we cannot assure you that we will identify suitable products or enter into such acquisitions on acceptable terms.

Acquisitions involve a number of operational risks, including:

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

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

If we make one or more significant acquisitions or enter into a significant collaboration in which the consideration includes cash, we may be required to use a substantial portion of our available cash and/or need to raise additional capital. For instance, in September and October of 2016, we borrowed \$30.0 million under our loan agreement with Hercules to fund the payment due under the license agreement with AstraZeneca, and this investment — as with any acquisition or collaboration — may not be successful.

Risks Related to Regulatory Matters

The manufacturing facilities of our third-party manufacturers are subject to significant government regulations and approvals, which are often costly and could result in adverse consequences to our business if we and our manufacturing partners fail to comply with the regulations or maintain the approvals.

Manufacturers of our product candidates are subject to CGMP and similar standards, and while we have policies and procedures in place to select manufacturers that adhere, and monitor their adherence to, such standards, they may nonetheless fail to do so. If one of them fails to obtain or maintain compliance or experiences problems in the scale-up of commercial production, the production of our product candidates could be interrupted, resulting in delays, additional costs or restrictions on the marketing or sale of our products. These manufacturers and their facilities will be subject to pre-approval CGMP inspection by the FDA and other regulatory authorities, and the findings of the CGMP inspection could result in a failure to obtain, or a delay in obtaining, regulatory approval. In addition, these manufacturers and their facilities will be subject to continual review and periodic inspections by the FDA and other regulatory authorities following regulatory approval, if any, of our product candidates. For instance, to monitor compliance with applicable regulations, the FDA routinely conducts inspections of facilities and may identify potential deficiencies. The FDA issues what are referred to as "FDA Form 483s" that set forth observations and concerns that are identified during its inspections. Failure to satisfactorily address the concerns or potential deficiencies identified in a Form 483 could result in the issuance of a warning letter, which is a notice of the issues that the FDA believes to be significant regulatory violations requiring prompt corrective actions. Failure to respond adequately to a warning letter, or to otherwise fail to comply with applicable regulatory requirements could result in enforcement, remedial and/or punitive actions by the FDA or other regulatory authorities.

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

If we obtain regulatory approval for ALIS 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 or other reasons, we or others may later discover that our products have adverse event 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 or clearance of the product and may require recall of product in distribution;
- Regulatory authorities may require the addition of labeling statements, such as black box or other warnings or contraindications, or the issuance of "Dear Doctor Letters" or similar communications to healthcare professionals;
- Regulatory authorities may impose additional restrictions on marketing and distribution of the products, or other risk management measures, such as a REMS;
- 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; and
- We could be subject to negative publicity, including communications issued by regulatory authorities.

Any of these events could prevent us from maintaining market acceptance of the affected product, cause substantial reduction in sales or substantially increase the costs of commercializing

our product candidates, cause significant financial losses or result in significant reputational damage.

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

Our prospects for generating revenue and achieving profitability depend heavily upon the availability of adequate reimbursement for the use of our approved product candidates from governmental and other third-party payers, both in the U.S. and in other markets. For instance, we expect a substantial majority of potential future ALIS revenues would come from Medicare reimbursement. Reimbursement by a third-party payer may depend upon a number of factors, including the third-party payer's determination that use of a product is:

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

Obtaining reimbursement approval for a product from each government or other third-party payer is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to each payer. We may not be able to provide data sufficient to gain acceptance with respect to reimbursement or we might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payers' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Even when a payer determines that a product is eligible for reimbursement, the payer may impose coverage limitations that preclude payment for some uses that are approved by the FDA or non-U.S. 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 U.S. healthcare industry and elsewhere on cost containment and value. We expect changes in the Medicare program and state Medicaid programs, as well as managed care organizations and other third-party payers, to continue to put pressure on pharmaceutical product pricing. For instance, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") expanded Medicare outpatient prescription drug coverage for the elderly through Part D prescription drug plans sponsored by private entities and authorized such plans to use formularies where they can limit the number of drugs that will be covered in any therapeutic class. The plans generally negotiate significant price concessions as a condition of formulary placement. The MMA also introduced a new reimbursement methodology based on average sales prices for physician-administered drugs, which is generally believed to have resulted in lower Medicare reimbursement for physician-administered drugs. These cost reduction initiatives and other provisions of this legislation provide additional pressure to contain and reduce drug prices and could decrease the coverage and price that we receive for any approved products and could seriously harm our business. Although the MMA applies only to drug benefits for Medicare

beneficiaries, private payers often follow Medicare coverage policy and payment limitations when setting their own reimbursement rates, and any reimbursement reduction resulting from the MMA may result in a similar reduction in payments from private payers. Additionally, the Patient Protection and Affordable Care Act ("ACA") revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states, and has imposed a significant annual fee on companies that manufacture or import branded prescription drug products. We believe it is likely that the ACA, or any legislation enacted to replace it, 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 and/or the U.S. President, 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 U.S., including Japan, Canada and the countries in the EU, pricing of pharmaceutical products is subject to governmental control. Evaluation criteria used by many EU government agencies for the purposes of pricing and reimbursement typically focus on a product's degree of innovation and its ability to meet a clinical need unfulfilled by currently available therapies. The ACA created a similar entity, the Patient-Centered Outcomes Research Institute ("PCORI") designed to review the effectiveness of treatments and medications in federally-funded health care programs. The PCORI began its first research initiatives recently, and an adverse result may result in a treatment or product being removed from Medicare or Medicare coverage. The decisions of such governmental agencies could affect our ability to sell our products profitably.

Government health care reform could increase our costs, and could materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

Our industry is highly regulated and changes in or revisions to laws and regulations that make gaining regulatory approval, reimbursement and pricing more difficult or subject to different criteria and standards may adversely impact our business, operations or financial results. For example, under the ACA, drug manufacturers are required to report information on payments or transfers of value to U.S. physicians and teaching hospitals as well as investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties. The reported data is posted in searchable form on a public website. In addition, some states, as well as other countries, including France, require the disclosure of certain payments to health care professionals. In the coming years, we expect additional and potentially substantial, changes to governmental programs that could significantly impact the success of our product candidates.

The Administration and the majority party in both Houses of Congress have indicated their ongoing desire to repeal the ACA. It is unclear whether, when and how that repeal may be effectuated and what the effect on the healthcare sector will be. The U.S. President has indicated an interest in having the federal government negotiate drug prices with pharmaceutical manufacturers. Changes to the ACA, to the Medicare or Medicaid programs, or to the ability of the federal government to negotiate drug prices, or other federal legislation regarding healthcare access, financing or legislation in individual states, could affect our business, financial condition, results of operations and prospects and the value of our common stock.

We will need approval from the FDA and other regulatory authorities in jurisdictions outside the U.S. 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 U.S. Patent and Trademark Office ("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. 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 ALIS could be delayed or interrupted, which would limit our ability to commercialize ALIS and generate revenues.

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, results of operations and prospects and the value of our common stock.

In the U.S., 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. 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 these laws. 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, and our business, financial condition, results of operations and prospects and the value of our common stock may be adversely affected. Our reputation could also suffer. 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.

Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. Health record privacy laws may limit access to information identifying those individuals who may be prospective users or prohibit contact with any persons enrolled in Medicare or Medicaid. There are ambiguities as to what is required to comply with these state requirements, and we could be subject to penalties if a state determines that we have failed to comply with an applicable state law requirement.

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.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain and involves complex legal, technical, scientific and factual questions, and our success depends in large part on our ability to protect our proprietary technology and to obtain patent protection for our products, prevent third parties from infringing on our patents, both domestically and internationally. We have sought to protect our proprietary position by filing patent applications in the U.S. and abroad related to our novel technologies and products that are important to our business. This process is expensive and time-consuming, and we may not be able to file and

prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technologies or from developing competing products and technologies.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Any conclusions we may reach regarding non-infringement, inapplicability or invalidity of a third party's intellectual property vis-à-vis our proprietary rights, or those of a licensor, 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 render these conclusions inaccurate. Our competitors may also be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

Additionally, patents issued to us or our licensors may be challenged, narrowed, invalidated, held to be unenforceable or circumvented through litigation, 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. U.S. patents and patent applications may also be subject to interference or derivation proceedings, and U.S. patents may be subject to re-examination proceedings, reissue, post-grant review and/or *inter partes* review in the PTO. Foreign patents may be subject to opposition or comparable proceedings in the corresponding foreign patent office, which could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. See *Intellectual Property — ARIKAYCE Patents and Trade Secrets* in Item 1 of Part I of our Annual Report on Form 10-K for the year ended December 31, 2016 (the "2016 Annual Report") for information on our European patent that was previously opposed, the decision of which is now under appeal by Generics (UK) Ltd, and our European patent that is currently being opposed by Generics (UK) Ltd.

Changes in either patent laws or in interpretations of patent laws in the U.S. and other countries may also diminish the value of our intellectual property or narrow the scope of our patent protection, including making it easier for competitors to challenge our patents. For example, the America Invents Act included a number of changes to established practices, including the transition to a first-inventor-to-file system and new procedures for challenging patents and implementation of different methods for invalidating patents.

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. Regulators also may disclose information we consider to be proprietary to third parties under certain circumstances, including in response to third-party requests for such disclosure under the Freedom of Information Act or comparable laws. Additionally, the FDA, as part of its Transparency Initiative continues to consider whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other

proprietary information, and it is not clear at the present time whether and how the FDA's disclosure policies may change in the future.

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

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

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

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. Any existing third-party patents, or patents that may later issue to third parties, could negatively affect our commercialization of ALIS, INS1007, INS1009 or any other product. For instance, PAH is a competitive indication with established products, including other formulations of tadalafil. Our supply of the active pharmaceutical ingredient for INS1009 is dependent upon a single supplier. The supplier owns patents on its manufacturing process, and we have filed patent applications for INS1009; however, a competitor in the PAH indication may claim that we or our supplier have infringed upon or misappropriated its proprietary rights. Moreover, in the event that we pursue approval of INS1009, or any other product candidate, via the 505(b)(2) regulatory pathway, we will be required to file a certification against any unexpired patents listed in the Orange Book for the third party drug we rely upon as part of our regulatory submission. This certification process may lead to litigation and could delay also launch of a product candidate.

In the event of a successful claim against us for infringement or misappropriation of a third party's proprietary rights, we may be required to take actions including but not limited to the following:

- Pay damages, including up to treble damages, royalties, and the other party's attorneys' fees, which may be substantial;
- Cease the development, manufacture, marketing and sale of products or use of processes that infringe the proprietary rights of others;
- Expend significant resources to redesign our products or our processes so that they do not infringe the proprietary rights of others, which may not be possible;
- Redesign our products or processes to avoid third-party proprietary rights, which means we may suffer significant regulatory delays associated with conducting additional clinical trials or other steps to obtain regulatory approval; and/or

- Obtain one or more licenses arising out of a settlement of litigation or otherwise from third parties which license(s) may not be available to us on acceptable terms or at all.

Such litigation, and any resulting resolution, could have a material adverse effect on our business, financial condition, results of operations and prospects and the value of our common stock.

Any lawsuits or other proceedings relating to infringement or enforcement by us or third parties of intellectual property rights or challenges to the scope and validity of such rights may be costly and time consuming.

We may have to undertake costly litigation or engage in other proceedings, such as interference or inter partes review, to enforce any patents issued or licensed to us, to confirm the scope and validity of our or a licensor's proprietary rights or to defend against allegations that we have infringed a third party's intellectual property rights. Such proceedings are likely to be time consuming and may divert management attention from operation of our business.

Certain of our existing license agreements include, and our future license agreements also may include, restrictions on our ability to freely develop or commercialize the product candidates that are subject to those agreements. If we fail to comply with our obligations under these agreements, or if these license agreements are terminated for other reasons, we could lose license rights that are important to our business.

We are a party to licensing agreements with PARI and AstraZeneca, which we view as material to our business. For additional information regarding the terms of these agreements, see *Business — License and Other Agreements* in Item 1 of Part I of our 2016 Annual Report. Under our license agreement with AstraZeneca, AstraZeneca retains a right of first negotiation pursuant to which it may exclusively negotiate with us before we can negotiate with a third party regarding any transaction to develop or commercialize INS1007, subject to certain exceptions. While this right of first negotiation is not triggered by a change of control, it may impede or delay our ability to consummate certain other transactions involving INS1007.

Additionally, if we fail to comply with our obligations under the agreements with PARI and AstraZeneca, our counterparty may have the right to take action against us, up to and including termination of the relevant license. For instance, under our licensing agreement with PARI, with respect to NTM, CF and bronchiectasis, we have specific obligations to use commercially reasonable efforts to achieve certain developmental and regulatory milestones by set deadlines. Additionally, for NTM, we are obligated to use commercially reasonable efforts to achieve certain commercial milestones in the U.S. and Europe. The consequences of our failing to use commercially reasonable efforts to achieve certain commercial milestones are context-specific, but include ending PARI's non-compete obligation, making the license non-exclusive and terminating the license, in each case with respect to the applicable indication. Similarly, under our license agreement with AstraZeneca, AstraZeneca may terminate our license to INS1007 if we fail to use commercially reasonable efforts to develop and commercialize a product based on INS1007, or we are subject to a bankruptcy or insolvency. Reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms and may materially harm our business.

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. In each of our potential product areas, we face substantial competition from pharmaceutical, biotechnology and other companies, universities and research institutions. Relative to us, most of these entities have substantially greater capital resources, research and development staffs, facilities and experience in conducting clinical studies and obtaining regulatory approvals, as well as in manufacturing and marketing pharmaceutical products. Many of our competitors may achieve product commercialization or obtain patent protection earlier than us. Furthermore, we believe that our competitors have used, and may continue to use, litigation to gain a competitive advantage. Our competitors may also use different technologies or approaches to the development of products similar to the products we are seeking to develop.

We expect that competing successfully 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. There are potential competitive products, both approved and in development, which include oral, systemic, or inhaled antibiotic products to treat chronic respiratory infections. For instance, certain entities have expressed interest in studying their products for NTM lung disease and are seeking to advance studies in NTM lung disease caused by mycobacterial species other than MAC; however, we are not aware that any such entities are currently conducting clinical trials for the treatment of refractory NTM lung disease caused by MAC or of any approved inhaled therapies specifically indicated for NTM lung disease in North America, Japan or Europe. If any of our competitors develops a product that is more effective, safe, tolerable or, convenient or less expensive than ALIS or our other product candidates, it would likely materially adversely affect our ability to generate revenues. We also may face lower priced generic competitors if third-party payers encourage use of generic or lower-priced versions of our product or if competing products are imported into the U.S. or other countries where we may sell ALIS.

In addition, there are other amikacin products that have been approved by the FDA, MHLW and other regulatory agencies for use in other indications, and physicians may elect to prescribe those products rather than ALIS to treat the indications for which ALIS may receive approval, which is commonly referred to as off-label use. Although regulations prohibit a drug company from promoting off-label use of its product, the FDA and other regulatory agencies do not regulate the practice of medicine and cannot direct physicians as to what product to prescribe to their patients. As a result, we would have limited ability to prevent any off-label use of a competitor's product to treat diseases for which we have received FDA or other regulatory agency approval, even if such use violates our patents or orphan drug exclusivity for the use of amikacin to treat such diseases. If we are unable to compete successfully, it will materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

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. The company that obtains the first regulatory 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 the EU with a term of ten years. See *Business — Government Regulation — Orphan Drugs* in Item 1 of Part I of our 2016 Annual Report for additional information. 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.

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

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

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our research and development program and manufacturing activities for ALIS and our other product candidates involve the controlled use of hazardous materials and chemicals. We generally contract with third parties for the disposal of these materials and wastes. Although we strive to comply with all pertinent regulations, we cannot eliminate the risk of environmental contamination, damage to facilities or injury to personnel from the accidental or improper use or control of these materials. In addition to any liability we could have for any misuse by us of hazardous materials and chemicals, we could also potentially be liable for activities of our CMOs or other third parties. Any such liability, or even allegations 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, which can lead to significant adverse publicity and obligations to pay damages. 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 and prospects and the value of our common stock.

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 and the value of our common stock.

We depend heavily on our management team and our principal clinical and commercial 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, clinical and commercial personnel, and on our ability to develop and maintain important relationships with commercial partners, leading research institutions and key distributors. We plan to hire additional personnel in anticipation of seeking regulatory approval for and commercial launch of ALIS.

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 clinical and commercial personnel from universities, research institutions, and other third parties. We cannot assure that we will attract and retain such persons or maintain such relationships. Our inability to retain and attract qualified employees would materially harm our business, financial condition, results of operations and prospects and the value of our common stock.

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

We expect that our potential expansion into areas and activities requiring additional expertise, such as further clinical trials, governmental approvals, manufacturing, sales, marketing and distribution will place additional requirements on our management, operational and financial resources. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these

growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees.

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

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

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

Our common stock is listed on the Nasdaq Global Select Market under the ticker symbol "INSM". The market price of our stock has been and may continue to be highly volatile, and could be subject to wide fluctuations in price in response to various factors, including those discussed herein, many of which are beyond our control. In addition, the stock market has from time to time experienced extreme price and volume fluctuations, which have particularly affected the market prices for emerging biotechnology and pharmaceutical companies like us, and which have often been unrelated to their operating performance. These broad market fluctuations may adversely affect the market price of our common stock. Historically, when the market price of a stock has been volatile, shareholders are more likely to institute securities and derivative class action litigation against the issuer of such stock. As described below, a securities class action lawsuit was initiated against us during 2016 following a decline in our stock price.

We, certain of our executive officers and directors and the underwriters from a prior securities offering are subject to a securities class action lawsuit, which may require significant management and board time and attention and significant expense to us and result in an unfavorable outcome, which could have a material adverse effect on our business, financial condition, results of operations and prospects and the value of our common stock.

We, certain of our executive officers and directors and the underwriters from a prior securities offering have been named as defendants in a securities class action lawsuit initially filed on July 15, 2016. The amended complaint, filed December 15, 2016, alleges that we and certain of our executive officers and directors violated Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended (the "Securities Act"), and that we, certain of our executive officers and the underwriters violated Section 10(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act") and Rule 10b-5 promulgated thereunder of the Exchange Act, by making materially false and misleading statements and omissions relating to the development of ALIS and/or related requests for regulatory approval. It also alleges that the defendant officers and directors violated Section 15 of the Securities Act and that the defendant officers violated Section 20(a) of the Exchange Act. For additional information, see Note 9, Commitments and Contingencies, in Item 1 of Part 1 of our Quarterly Report on Form 10-Q for the quarter ended June 30, 2017. While we believe that we have substantial legal and factual defenses to the claims in the class action and intend to vigorously defend the case, this lawsuit could divert our management's and board's attention from other business matters, the outcome of the pending litigation is difficult to predict and quantify, and the defense against the underlying claims will likely be costly. The ultimate resolution of this matter could result in payments of monetary damages or other costs, materially and adversely affect our business, financial condition and results of operations, and adversely affect our reputation and prospects, and consequently, could negatively impact the value of our common stock.

We have insurance policies related to the risks associated with our business, including directors' and officers' liability insurance policies. However, there is no assurance that our insurance coverage will be sufficient or that our insurance carriers will cover all claims in that litigation. If we are not successful in our defense of the claims asserted in the putative action and those claims are not covered by insurance or exceed our insurance coverage, we may have to pay damage awards, indemnify our executive officers and directors from damage awards that may be entered against them and pay the costs and expenses incurred in defense of, or in any settlement of, such claims. In addition, we are indemnifying the underwriters that are party to this action against the claims asserted against them, and these costs and expenses might not be covered by insurance.

In addition, there is the potential for additional shareholder litigation against us, and we could be materially and adversely affected by such matters.

Certain provisions of Virginia law, our articles of incorporation and amended and restated bylaws and arrangements between us and our employees 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, our articles of incorporation and amended and restated bylaws and arrangements with our employees 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 or arrangements include:

- The ability to issue preferred stock with rights senior to those of our common stock without any further vote or action by the holders of our common stock. The issuance of preferred stock could decrease the amount of earnings and assets available for distribution to the holders of our common stock or could adversely affect the rights and powers, including voting rights, of the holders of our common stock. In certain circumstances, such issuance could have the effect of decreasing the market price of our 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.
- The 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.
- The prohibition against 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 certain criteria are met.
- In addition to severance agreements with our officers and provisions in our incentive plans that permit acceleration of equity awards upon a change in control, a severance plan for eligible full-time employees that provides such employees with severance equal to six months of their then-current base salaries in connection with a termination of employment without cause upon, or within 18 months following, a change in control.

We previously had a shareholder rights plan, or "poison pill", 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

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

We currently have limited operations outside of the U.S. As of June 30, 2017, we had 24 employees located in Europe, and we have suppliers located around the world. In order to meet our long-term goals, we will need to grow our international operations over the next several years, including in Japan, and continue to source material used in the manufacture of our product candidates from abroad. Consequently, we are and will continue to be subject to additional risks related to operating in foreign countries, including:

- Our limited experience operating our business internationally;
- An inability to achieve the optimal pricing and reimbursement for ALIS or subsequent changes in reimbursement, pricing and other regulatory requirements;
- Any implementation of, or changes to, tariffs, trade barriers and other import-export regulations in the U.S. or other countries in which we operate;
- Unexpected adverse events related to ALIS or our other product candidates occurring in foreign markets that we have not experienced in the U.S.;
- Economic and political conditions, including geopolitical events, such as war and terrorism, foreign currency fluctuations and inflation, which could result in increased or unpredictable operating expenses and reduced revenues and other obligations incident to doing business in, or with a company located in, another country;
- Changes resulting from (i) the uncertainty and instability in economic and market conditions caused by the UK's vote to exit the European Union; and (ii) the uncertainty regarding how the UK's access to the EU Single Market and the wider trading, legal, regulatory and labor environments will be impacted by the UK's vote to exit the European Union, including the resulting impact on our business; and
- Compliance with foreign or U.S. laws, rules and regulations, including data privacy requirements, labor relations laws, tax laws, anticompetition regulations, import, export and trade restrictions, anti-bribery/anti-corruption laws, regulations or rules, which could lead to actions by us or our licensees, distributors, manufacturers, other third parties who act on our behalf or with whom we do business in foreign countries or our employees who are working abroad that could subject us to investigation or prosecution under such foreign or U.S. laws.

These and other risks associated with our international operations may materially adversely affect our business, financial condition, results of operations and prospects and the value of our common stock.

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

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in our operations, it could result in a material adverse effect on our business operations, including a material disruption of our drug

development programs. Unauthorized disclosure of sensitive or confidential client or employee data, whether through breach of computer systems, systems failure, employee negligence, fraud or misappropriation, or otherwise, could damage our reputation. Similarly, unauthorized access to or through our information systems and networks, whether by our employees or third parties, could result in negative publicity, legal liability and damage to our reputation. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Although we have general liability insurance coverage, including coverage for errors or omissions, our insurance may not cover all claims, continue to be available on reasonable terms or be sufficient in amount to cover one or more large claims; additionally, the insurer may disclaim coverage as to any future claim. The successful assertion of one or more large claims against us that exceed or are not covered by our insurance coverage or changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could have a material adverse effect on our business, financial condition, results of operations and prospects and the value of our common stock.

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

Our operations are subject to anti-corruption laws, including the U.S. Foreign Corrupt Practices Act ("FCPA"), the UK Bribery Act and other anticorruption laws that apply in countries where we do business. The FCPA, UK Bribery Act and these other laws generally prohibit us, our employees and our intermediaries from making prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. We have conducted the CONVERT study at more than 125 sites in 18 countries, and we are conducting the 312 study and plan to conduct the WILLOW study, our global phase 2 study of INS1007 in non-CF bronchiectasis, at a broad range of trial sites around the world. Certain of these jurisdictions pose a risk of potential FCPA violations, and we have relationships with third parties whose actions could potentially subject us to liability under the FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted.

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

We may not be effective in ensuring our compliance with all applicable anticorruption laws, including the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of

operations and prospects and the value of our common stock. Likewise, even an investigation by U.S. or foreign authorities of potential violations of the FCPA other anti-corruption laws or Trade Control laws could have an adverse impact on our reputation, business, financial condition, results of operations and prospects and the value of our common stock.

Risks Related to This Offering

Our management will have broad discretion over the actual amounts and timing of the expenditures of the proceeds we receive in this offering and might not apply the proceeds in ways that enhance our operating results or increase the value of your investment.

We intend to use the net proceeds from this offering to fund ongoing and future clinical development of ALIS for patients with refractory NTM lung disease caused by MAC and our efforts to obtain potential regulatory approvals for, and, if approved, commercialize ALIS in its approved indication; invest in increased third-party manufacturing capacity for and commercial inventory production of ALIS in anticipation of possible commercial launch, initially in the United States and subsequently in Japan and other countries; fund further clinical development of INS1007; and fund working capital, potential debt repayment, capital expenditures, general research and development, and for other general corporate purposes, which may include the acquisition or in-license of additional compounds, product candidates, technology or businesses. This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the success of our clinical development efforts and any potential commercialization efforts, as well as any strategic transactions that we may enter into with third parties, and any unforeseen cash needs. Because of the number and variability of factors that will determine our use of the proceeds from this offering, their ultimate use may vary substantially from their currently intended use. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering and could spend the proceeds in ways that do not necessarily improve our financial condition or operating results or enhance the value of our common stock and your investment therein. Additionally, until the net proceeds we receive are used, they may be placed in investments that do not produce income or that lose value. See "Use of Proceeds" for additional information.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock as of June 30, 2017. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share immediately after this offering. After giving effect to the sale of _____ shares of our common stock in this offering at the public offering price of \$ _____ per share and based on our net tangible book value as of June 30, 2017 of \$0.40 per share, if you purchase shares of common stock in this offering, you will suffer substantial and immediate dilution of \$ _____ per share in the net tangible book value of the common stock. Further dilution of your investment will result from, among other things, the future exercise of outstanding options and vesting of restricted stock units. See "Dilution" for a more detailed description of the dilution investors purchasing shares of our common stock in the offering will incur.

A significant portion of our total outstanding shares may be sold into the market at any time, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. Such sales, or the perception in the market that the holders of a large number of such shares intend to sell, could reduce the market price of our common stock significantly. Upon the completion of this offering, we and our executive officers and directors will be subject to lock-up agreements with the managers of the underwriters that prohibit us and such executive officers and directors, subject to certain exceptions or receipt of the prior written consent of the managers, from disposing or pledging, or hedging against, our common stock or securities convertible into or exchangeable for shares of our common stock for a period of 90 days, with respect to us, and 60 days with respect to our executive officers and directors, after the date of this prospectus supplement. However, all of the shares sold in this offering and the remaining shares of our common stock outstanding immediately prior to this offering will not be subject to lock-up agreements with the managers of the underwriters and, except to the extent such shares are held by our affiliates, will be freely tradable without restriction. In addition, the managers of the underwriters may, in their discretion, release the lock-up restrictions described above at any time without notice.

USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering will be approximately \$ _____ million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that the net proceeds from this offering will be approximately \$ _____ million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We currently plan to use the net proceeds from this offering as follows:

- to fund ongoing and future clinical development of ALIS for patients with refractory NTM lung disease caused by MAC and our efforts to obtain potential regulatory approvals for and, if approved, commercialize ALIS in its approved indication;
- to invest in increased third-party manufacturing capacity for and commercial inventory production of ALIS in anticipation of possible commercial launch, initially in the United States and subsequently in Japan and other countries;
- to fund further clinical development of INS1007; and
- to fund working capital, potential debt repayment, capital expenditures, general research and development, and for other general corporate purposes, which may include the acquisition or in-license of additional compounds, product candidates, technology or businesses.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the success of our clinical development efforts and any potential commercialization efforts, as well as any strategic transactions that we may enter into with third parties, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We have no current understandings, agreements or commitments for any material acquisitions or licenses of any compounds, product candidates, technology or businesses.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and the net tangible book value per share of our common stock immediately after this offering.

Our historical net tangible book value as of June 30, 2017 was \$25.2 million, or \$0.40 per share of our common stock, based upon 62,376,416 shares outstanding on June 30, 2017. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding as of June 30, 2017. After reflecting the sale of _____ shares of our common stock offered by us at the assumed public offering price of \$ _____ per share, less underwriting discounts and commissions and estimated offering expenses, our as-adjusted net tangible book value would have been approximately \$ _____ million, or approximately \$ _____ per share of common stock based upon _____ shares outstanding. This represents an immediate increase in net tangible book value of \$ _____ per share to our existing shareholders and an immediate dilution in net tangible book value of \$ _____ per share to investors purchasing shares of our common stock in this offering. The following table illustrates this calculation on a per share basis:

Assumed public offering price per share	\$
Net tangible book value per share as of June 30, 2017	\$ 0.40
Increase in net tangible book value per share attributable to investors purchasing shares of our common stock in this offering	\$ _____
As-adjusted net tangible book value per share after this offering	\$ _____
Dilution per share to investors purchasing shares of our common stock in this offering	\$ _____

The number of shares of our common stock to be outstanding immediately after this offering excludes:

- 8,621,451 shares of our common stock issuable upon the exercise of stock options outstanding as of June 30, 2017 at a weighted average exercise price of \$13.87 per share;
- 46,914 shares of our common stock issuable pursuant to unvested restricted stock units outstanding as of June 30, 2017 at a weighted average grant price of \$17.16; and
- 4,978,554 shares of our common stock reserved for issuance under our 2017 Incentive Plan, plus any shares subject to outstanding awards as of May 18, 2017 under our 2015 Incentive Plan and 2013 Incentive Plan that subsequently are cancelled, terminated unearned, expired, forfeited, lapsed for any reason or are settled in cash without the delivery of shares.

In addition, the amounts in the table above assume no exercise by the underwriters of their option to purchase additional shares of our common stock.

Investors purchasing shares of our common stock in this offering will experience further dilution upon the future exercise of outstanding options and vesting of restricted stock units as well as when new equity awards are made and either are exercised or become vested under our 2017 Incentive Plan. Furthermore, subject to the terms of our lockup agreement with the managers of the underwriters, as described in "Underwriting", we may choose to raise additional capital through the sale of additional securities due to market conditions or strategic considerations even if we believe we have sufficient funds on hand for our current or future operating plans. To the extent that we raise additional capital in this manner, the issuance of such securities could result in further dilution to investors purchasing shares of our common stock in this offering.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, to be dated the date of this prospectus supplement, between us, Goldman Sachs & Co. LLC and Leerink Partners LLC, as the managers of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

<u>Underwriter</u>	<u>Number of Shares</u>
Goldman Sachs & Co. LLC	
Leerink Partners LLC	
Evercore Group L.L.C.	
Stifel, Nicolaus & Company, Incorporated	
Total	

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below, unless and until the option is exercised.

The underwriters have an option to buy up to an additional \$37,500,000 of our common stock to cover sales by them of a greater number of shares than the total number set forth in the table above. They may exercise that option for 30 days from the date of this prospectus supplement. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in the same proportion as set forth in the table above.

The following table shows the public offering price of the common stock being offered hereby, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	<u>Per Share</u>	<u>Total</u>	
		<u>No Exercise</u>	<u>Full Exercise</u>
Public offering price	\$	\$	\$
Underwriting discounts and commissions	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$. We have agreed to reimburse the underwriters in an amount not to exceed \$10,000 for expenses related to the offering's compliance with the rules of the Financial Industry Regulatory Authority. We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

Shares sold by the underwriters to the public will initially be offered at the initial public offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to certain dealers may be sold at a discount of up to \$ per share from the initial public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

Restrictions on Sales of Similar Securities

In connection with this offering, we and each of our directors and executive officers have agreed, subject to certain exceptions, that, for a period of 90 days, with respect to us, and 60 days with respect to our executive officers and directors, after the date of this prospectus supplement, we and they will not, without the prior written consent of Goldman Sachs & Co. LLC and Leerink Partners LLC, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend, or otherwise transfer or dispose of, directly or indirectly, any shares of common stock beneficially owned by them or any securities so owned convertible into or exercisable or exchangeable for common stock; or enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock.

Stabilization

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short-covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our common stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of our common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Electronic Distribution

A prospectus supplement and accompanying prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the

underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of our common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus supplement and accompanying prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus supplement or the accompanying prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to us and to persons and entities with relationships with us, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to assets, securities and/or instruments of Insmid (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Selling Restrictions

Other than in the United States, no action has been taken by us or any underwriter that would permit a public offering of the shares of common stock offered by this prospectus supplement in any jurisdiction where action for that purpose is required. Shares of common stock offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such shares of common stock be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to this offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any shares of common stock offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), an offer to the public of our common shares may not be made in that Relevant Member State, except that an offer to the public in that

Relevant Member State of our common shares may be made at any time under the following exemptions under the Prospectus Directive:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the managers for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of our common shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to public" in relation to our common shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common shares to be offered so as to enable an investor to decide to purchase our common shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State, and the expression "Prospectus Directive" means Directive 2003/71/EC (as amended, including by Directive 2010/73/EU) and includes any relevant implementing measure in the Relevant Member State.

United Kingdom

In the United Kingdom, this prospectus supplement is only addressed to and directed at qualified investors who are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order"); or (ii) high net worth entities and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). In the United Kingdom, any investment or investment activity to which this prospectus relates is available only to relevant persons and will only be engaged with relevant persons. Any person in the United Kingdom who is not a relevant person should not act or rely on this prospectus or any of its contents.

Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) ("Companies (Winding Up and Miscellaneous Provisions) Ordinance") or which do not constitute an offer to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) ("Securities and Futures Ordinance"), or (ii) to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong), other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA")) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for six months after that corporation has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation's securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore ("Regulation 32").

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for six months after that trust has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended) (the "FIEA"). The shares may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

Canada

The shares may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts ("NI 33-105"), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

**MATERIAL UNITED STATES FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS
FOR NON-U.S. HOLDERS OF SHARES OF OUR COMMON STOCK**

The following discussion summarizes certain material United States federal income and estate tax considerations relating to the purchase, ownership, and disposition of shares of our common stock by a non-U.S. holder (as defined below) that acquires our common stock in this offering and holds it as a capital asset. This discussion is based on the tax laws of the United States, including the Code, Treasury regulations promulgated or proposed thereunder, and administrative and judicial interpretations thereof, all as in effect on the date of this prospectus supplement. These tax laws are subject to change, possibly with retroactive effect, and subject to differing interpretations that could affect the tax consequences described herein.

For purposes of this discussion, a "non-U.S. holder" is a beneficial owner of our common stock that, for United States federal income tax purposes, is:

- a non-resident alien;
- a foreign corporation (or other entity taxable as a corporation);
- an estate the income of which is not subject to United States federal income taxation regardless of its source; or
- a trust that does not have in effect a valid election under the Treasury regulations to be treated as a United States person and either (1) no court within the United States is able to exercise primary supervision over the trust's administration or (2) no United States person has the authority to control all substantial decisions of that trust.

This discussion does not address all aspects of United States federal income and estate taxation that may be applicable to non-U.S. holders in light of their particular circumstances or status (including, for example, financial institutions, broker-dealers, insurance companies, partnerships or other pass-through entities, certain United States expatriates, tax-exempt organizations, pension plans, persons in special situations, such as those that have elected to mark securities to market or that hold shares of our common stock as part of a straddle, hedge or other integrated investment, and foreign governments or agencies).

If a partnership (including any entity or arrangement treated as a partnership for United States federal income tax purposes) purchases, owns, or disposes of our common stock, the tax treatment of a person treated as a partner in the partnership for United States federal income tax purposes generally will depend on the status of the partner and the activities of the partnership. Partnerships (and other entities or arrangements so treated for United States federal income tax purposes) and their partners should consult their own tax advisors.

This discussion addresses only non-U.S. holders and does not discuss any tax considerations other than United States federal income tax and certain United States federal estate tax considerations. Prospective investors are urged to consult their own tax advisors regarding the United States federal, state, and local, and foreign tax consequences of the purchase, ownership, and disposition of our common stock, including the effect of any applicable income or estate tax treaty.

Dividends

We have never declared or paid cash dividends on our common stock. We anticipate that we will retain all earnings, if any, to support our operations and to finance the growth and development of our business for the foreseeable future.

If we do make a distribution of cash or property with respect to our common stock, any such distribution generally will constitute a dividend for United States federal income tax purposes to the extent of our current or accumulated earnings and profits, as determined under United States federal income tax principles. Any distribution in excess of our current or accumulated earnings and profits will be treated, first, as a tax-free return of the non-U.S. holder's capital, up to the holder's adjusted tax basis in shares of our common stock, and thereafter, as capital gain subject to the tax treatment described below in "Gain on Sale, Exchange or Other Taxable Disposition".

Any dividends paid to a non-U.S. holder generally will be subject to withholding tax at a 30% rate or at a lower rate under an applicable income tax treaty between the United States and the non-U.S. holder's country of residence. In order to receive a reduced treaty withholding tax rate and to avoid backup withholding, as described below, a non-U.S. holder must furnish to us or our paying agent a properly executed Internal Revenue Service Form W-8BEN or Form W-8BEN-E (or other applicable form) prior to payment of the dividend, certifying under penalties of perjury that the non-U.S. holder is entitled to a reduction in withholding under an applicable income tax treaty. A non-U.S. holder that holds our common stock through a financial institution or other agent will be required to provide appropriate documentation to the financial institution or other agent, which then will be required to provide certification to us or our paying agent either directly or through other intermediaries. A non-U.S. holder that is eligible for a reduced rate of withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by filing a refund claim with the Internal Revenue Service.

A non-U.S. holder is exempt from the withholding tax described above if the dividend is "effectively connected" with the conduct of a trade or business in the United States of the non-U.S. holder (and, if an applicable income tax treaty so provides, attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States) and the non-U.S. holder furnishes to us or our paying agent an Internal Revenue Service Form W-8ECI (or applicable successor form), certifying under penalties of perjury that the dividend is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States (and, if an applicable income tax treaty so provides, attributable to a permanent establishment or fixed base maintained in the United States). "Effectively connected" dividends will generally be subject to United States federal income tax at the graduated rates that also apply to U.S. persons. A corporate non-U.S. holder may, under certain circumstances, be subject to an additional branch profits tax at a 30% rate (or at a lower rate under an applicable income tax treaty) with respect to its "effectively connected" dividends.

Gain on Sale, Exchange or Other Taxable Disposition

Subject to the discussion below under "FATCA Withholding" and "Information Reporting and Backup Withholding", a non-U.S. holder generally will not be subject to United States federal income tax or withholding tax on gain realized upon a sale, exchange or other taxable disposition of shares of our common stock (including a redemption, but only if the redemption would be treated as a sale or exchange rather than a distribution for United States federal income tax purposes) unless:

- the gain is "effectively connected" with the conduct of a trade or business of the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, the gain is attributable to a permanent establishment or fixed base maintained in the United States), in which case the non-U.S. holder generally will be subject to United States federal income tax on a net income basis with respect to such gain in the same manner as if such holder were a resident of the United States and, if the non-U.S. holder is a corporation for United States federal income tax purposes, will be subject to an additional "branch profits tax" at a 30% rate (or at a lower rate under an applicable income tax treaty);

- the non-U.S. holder is an individual who is present in the United States for 183 or more days in the taxable year of the disposition and meets certain other conditions, in which case the non-U.S. holder generally will be subject to United States federal income tax at a 30% rate (or at a lower rate under an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S.-source capital losses for the year; or
- we are or have been a "United States real property holding corporation" ("USRPHC") at any time within the shorter of the five-year period preceding the disposition and the non-U.S. holder's holding period for our common stock (the "relevant period") and the non-U.S. holder (i) disposes of our common stock during a calendar year when our common stock is no longer regularly traded on an established securities market or (ii) owned (directly, indirectly, and constructively) more than 5% of our common stock at any time during the relevant period, in which case such a non-U.S. holder will be subject to tax on the gain on the disposition of shares of our common stock generally as if the gain were effectively connected with the conduct of a trade or business in the United States, except that the "branch profits tax" will not apply.

We believe we currently are not, and we do not anticipate becoming, a USRPHC for United States federal income tax purposes. Generally, a corporation is a USRPHC only if the fair market value of its United States real property interests (as defined in the Code) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests and its other assets used or held for use in a trade or business.

FATCA Withholding

Sections 1471 through 1474 of the Code (commonly referred to as the Foreign Account Tax Compliance Act ("FATCA")) impose a 30% withholding tax on dividends on our common stock and gross proceeds from the sale or other disposition of our common stock on or after January 1, 2019 to a foreign entity unless:

- the foreign entity (i) is a "foreign financial institution" that undertakes specified due diligence, reporting, withholding and certification obligations or (ii) in the case of a foreign financial institution that is a resident in a jurisdiction that has entered into an intergovernmental agreement with the United States relating to FATCA, complies with the diligence and reporting requirements of the intergovernmental agreement and local implementing rules;
- the foreign entity is not a "foreign financial institution" and identifies certain of its United States investors; or
- the foreign entity otherwise is exempted from withholding.

An intergovernmental agreement between the United States and an applicable foreign country where a foreign entity is a resident may modify the requirements under FATCA in this paragraph and, under certain circumstances, can eliminate FATCA withholding tax. Under certain circumstances, a non-U.S. holder will be eligible for refunds or credits of withholding taxes imposed under FATCA by filing a United States federal income tax return. Prospective investors should consult their tax advisors regarding the effect of FATCA on their ownership and disposition of our common stock.

Information Reporting and Backup Withholding

Except as described below, a non-U.S. holder generally will be exempt from backup withholding and information reporting requirements with respect to dividend payments and the payment of the proceeds from the sale of shares or our common stock effected at a United States

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office of a broker, as long as the payor or broker does not have actual knowledge or reason to know that the holder is a United States person and has furnished to the payor or broker:

- a valid Internal Revenue Service Form W-8BEN or Form W-8BEN-E on which the non-U.S. holder certifies, under penalties of perjury, that it is a non-United States person; or
- other documentation upon which it may rely to treat the payments as made to a non-United States person in accordance with Treasury regulations,

or the non-U.S. holder otherwise establishes an exemption.

However, we must report annually to the Internal Revenue Service and to non-U.S. holders the amount of dividends paid to non-U.S. holders and the tax withheld with respect to such dividends, regardless of whether withholding was required. Copies of the information returns reporting such dividends and withholding may also be made available to the tax authorities in the country in which the respective non-U.S. holder resides under the provisions of an applicable income tax treaty.

Payment of the proceeds from the sale of our common stock effected at a foreign office of a broker generally will not be subject to information reporting or backup withholding. However, a sale of our common stock by a non-U.S. holder that is effected at a foreign office of a broker will be subject to information reporting and backup withholding if:

- the proceeds are transferred to an account maintained by the non-U.S. holder in the United States;
- the payment of proceeds or the confirmation of the sale is mailed to the non-U.S. holder at a United States address; or
- the sale has some other specified connection with the United States as provided in the Treasury regulations,

unless the broker does not have actual knowledge or reason to know that the holder is a United States person and the documentation requirements described above are met or the non-U.S. holder otherwise establishes an exemption.

In addition, a sale of shares of our common stock will be subject to information reporting if it is effected at a foreign office of a broker that is:

- a United States person;
- a "controlled foreign corporation" for United States federal income tax purposes;
- a foreign person 50% or more of whose gross income is effectively connected with the conduct of a United States trade or business for a specified three-year period; or
- a foreign partnership, if at any time during its tax year (a) one or more of its partners are "U.S. persons", as defined in the Treasury regulations, who in the aggregate hold more than 50% of the income or capital interest in the partnership, or (b) such foreign partnership is engaged in the conduct of a trade or business in the United States,

unless the broker does not have actual knowledge or reason to know that the holder is a United States person and the documentation requirements described above are met or an exemption is otherwise established. Backup withholding will apply if the sale is subject to information reporting and the broker has actual knowledge that the holder is a United States person.

Backup withholding is not an additional tax. A non-U.S. holder generally may obtain a refund of any amounts withheld under the backup withholding rules that exceed the non-U.S. holder's income tax liability by filing a refund claim with the Internal Revenue Service.

Federal Estate Taxes

The estates of nonresident alien decedents generally are subject to United States federal estate tax on property with a United States situs. Because we are a United States corporation, our common stock will be United States situs property and therefore will be included in the taxable estate of a nonresident alien decedent at the time of the decedent's death, unless an applicable estate tax treaty between the United States and the decedent's country of residence provides otherwise. An estate tax credit is available to reduce the net tax liability of a nonresident alien's estate, but the estate tax credit for a nonresident alien is generally much smaller than the applicable credit for computing the estate tax of a United States resident. Nonresident aliens should consult their personal tax advisors regarding the United States federal estate tax consequences of owning our common stock.

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Covington & Burling LLP, Washington, D.C. The validity of the common stock being offered hereby will be passed upon for us by Hunton & Williams LLP, Richmond, Virginia. Ropes & Gray LLP, Boston, Massachusetts, is counsel for the underwriters in connection with this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, and the effectiveness of our internal control over financial reporting as of December 31, 2016, as set forth in their reports, which are incorporated herein by reference. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring to those publicly available documents. The information that we incorporate by reference is considered to be part of this prospectus supplement. We incorporate by reference the documents listed below (File No. 000-30739) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of this prospectus supplement and the date this offering is terminated:

- Annual Report on Form 10-K for the year ended December 31, 2016;
- Quarterly Reports on Form 10-Q for the quarters ended March 31, 2017 and June 30, 2017;
- Current Reports on Form 8-K, filed with the SEC on May 19, 2017 and May 22, 2017; and
- Description of our common stock contained in our registration statement on Form 8-A, dated June 1, 2000, including any amendment or report subsequently filed for the purpose of updating such description.

You may access our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statement, and other information, if any, we file with or furnish to the SEC free of charge at the SEC's website (www.sec.gov) or our website (www.insmed.com) as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus supplement.

You may also request a copy of our SEC filings at no cost, by telephoning or writing us at the following telephone number or address:

Insmmed Incorporated
10 Finderne Avenue, Building 10
Bridgewater, New Jersey 08807
Attention: Christine Pellizzari, General Counsel and Corporate Secretary
(908) 977-9900

PROSPECTUS



Common Stock

We may from time to time offer to sell common stock in amounts, at prices and on terms described in one or more supplements to this prospectus. This prospectus describes some of the general terms that may apply to an offering of our common stock. Each time we sell common stock pursuant to this prospectus, the specific terms and any other information relating to a specific offering will be set forth in a post-effective amendment to the registration statement of which this prospectus is a part, in a prospectus supplement or in one or more documents incorporated by reference in this prospectus. The amendment, supplement or incorporated document(s), as applicable, may also add to, update or change information contained in this prospectus.

Our common stock may be offered and sold in the same offering or in separate offerings to or through one or more underwriters, dealers, and agents, directly to purchasers, or through a combination of these methods. The names and compensation of any underwriter, dealer or agent involved in the sale of our common stock will be described in the applicable prospectus supplement. See "Plan of Distribution" on page 5 of this prospectus for additional information.

You should read this prospectus, any applicable prospectus supplement and any incorporated documents carefully before you invest in our common stock. This prospectus is not an offer to sell our common stock, and it is not soliciting an offer to buy our common stock, in any state or other jurisdiction where the offer or sale is not permitted.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "INSM." On May 17, 2017, the last reported sale price for our common stock was \$17.16. You are encouraged to obtain current market prices for shares of our common stock.

Our principal executive offices are located at 10 Finderne Avenue, Building 10, Bridgewater, NJ 08807, and our telephone number is (908) 977-9900.

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors incorporated in this prospectus by reference and described under the heading "Risk Factors" on page 2 of this prospectus.

Neither the Securities and Exchange Commission ("SEC") nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is May 19, 2017.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the SEC, utilizing a "shelf" registration process as a "well-known seasoned issuer," as defined in Rule 405 under the Securities Act. Under this shelf registration process, we may offer and sell from time to time in one or more offerings the common stock described in this prospectus.

This prospectus provides you with a general description of our common stock. Each time we sell shares of our common stock, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement, or information incorporated by reference in this prospectus or any prospectus supplement that is of a more recent date, may also add to, update or change information contained in this prospectus. To the extent that any statement that we make in a prospectus supplement or incorporate by reference from a future SEC filing is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the prospectus supplement or such incorporated document. This prospectus may not be used to consummate a sale of our common stock unless it is accompanied by a prospectus supplement. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to an offering of our common stock. You should carefully read this prospectus, any applicable prospectus supplement and any relevant free writing prospectus, together with the information incorporated herein by reference, prior to making any decision regarding an investment in our common stock.

You should rely only on the information contained or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. We are not making offers to sell or seeking offers to buy shares of our common stock in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of the respective dates of such documents. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to "Insmmed", the "Company", "we", "us" and "our" refer to Insmmed Incorporated, a Virginia corporation, together with its consolidated subsidiaries. Insmmed and ARIKAYCE are trademarks of Insmmed Incorporated. Our logos and trademarks are the property of Insmmed. All other brand names or trademarks appearing in this prospectus are the property of their respective holders. Use or display by us of other parties' trademarks or trade dress in this prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

INSMED INCORPORATED

We are a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. We were incorporated in the Commonwealth of Virginia on November 29, 1999. On December 1, 2010, we completed a business combination with Transave, Inc., a privately held New Jersey based company focused on the development of differentiated and innovative inhaled pharmaceuticals for the site specific treatment of serious lung diseases.

Our lead product candidate is ARIKAYCE, or liposomal amikacin for inhalation, which is in late-stage development for adult patients with treatment refractory nontuberculous mycobacteria lung disease caused by *Mycobacterium avium* complex, a rare and often chronic infection that is capable of causing irreversible lung damage and can be fatal. Our earlier clinical-stage pipeline includes INS1007 and INS1009. INS1007 is a novel oral, reversible inhibitor of dipeptidyl peptidase 1, an enzyme responsible for activating neutrophil serine proteases, which are implicated in the pathology of chronic inflammatory lung diseases, such as non-cystic fibrosis bronchiectasis. INS1009 is an inhaled nanoparticle formulation of a treprostinil prodrug that may offer a differentiated product profile for rare pulmonary disorders, including pulmonary arterial hypertension.

Our principal executive offices are located at 10 Finderne Avenue, Building 10, Bridgewater, NJ 08807, and our telephone number is (908) 977-9900. Our Internet address is www.insmed.com. The information on our web site is not incorporated by reference into this prospectus or any applicable prospectus supplement and should not be considered to be part of this prospectus or any applicable supplement.

RISK FACTORS

An investment in our common stock involves risks. Prior to making a decision about investing in our common stock, you should carefully consider the specific risks discussed under "Risk Factors" in our Annual Report on Form 10-K for our most recent fiscal year, as updated by our Quarterly Reports on Form 10-Q and other SEC filings subsequent thereto, pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and in any applicable prospectus supplement. The risks and uncertainties described in any applicable prospectus supplement and in our SEC filings are not the only ones facing us. Each of these risks could materially and adversely affect our business, results of operations and financial condition, resulting in a decline in the trading price of our common stock and a complete or partial loss of your investment.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains, and the information incorporated by reference herein and any applicable prospectus supplement may contain, forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. "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 such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," "continues," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) identify forward looking statements.

Forward looking statements are based on our current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause our actual results, performance and achievements and the timing of certain events to differ materially from the results,

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performance, achievements or timing discussed, projected, anticipated or indicated in any forward looking statements. Such factors include, among others, the following:

- uncertainties in the research and development of our existing product candidates, including due to delays in patient enrollment or failure of our preclinical studies or clinical trials to satisfy pre-established endpoints;
- failure to develop, or to license for development, additional product candidates, including a failure to attract experienced third party collaborators;
- failure to obtain, or delays in obtaining, regulatory approval from the United States Food and Drug Administration, the European Medicines Agency, and other regulatory authorities for our product candidates or their delivery devices, including due to insufficient clinical data or selection of endpoints that are not satisfactory to regulators;
- failure of third parties on which we are dependent to conduct our clinical trials and to manufacture sufficient quantities of our product candidates for clinical or commercial needs;
- failure to comply with license agreements that are critical for our product development, including our license agreements with PARI Pharma GmbH and AstraZeneca AB;
- lack of safety and efficacy of our product candidates;
- inaccuracies in our estimate of the size of the potential markets for our product candidates;
- failure to maintain regulatory approval for our product candidates, once received, due to a failure to satisfy post-approval regulatory requirements, such as the need for post-clinical trials;
- uncertainties in the rate and degree of market acceptance of product candidates, if approved;
- uncertainties in the timing, scope and rate of reimbursement for our product candidates;
- competitive developments affecting our product candidates;
- inaccurate estimates regarding our future capital requirements, including those necessary to fund milestone payments or royalties owed to third parties;
- inability to repay our existing indebtedness or to obtain additional financing when needed;
- failure to obtain, protect and enforce our patents and other intellectual property;
- inability to create an effective direct sales and marketing infrastructure or to partner with a third party that offers such an infrastructure for distribution of our product candidates;
- the cost and potential reputational damage resulting from litigation to which we are a party, including, without limitation, the class action lawsuit pending against us;
- failure to comply with the laws and regulations that impact our business;
- loss of key personnel; and
- changes in laws and regulations applicable to our business, including those related to pricing and reimbursement of our product candidates.

The factors, risks and uncertainties referred to above and others are more fully described under the heading "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, as updated from time to time in our Quarterly Reports on Form 10-Q and other SEC filings subsequent thereto, including any applicable prospectus supplement. We caution readers not to place undue reliance on any such forward-looking statements, which speak only as

of the date they were made. We disclaim any obligation, except as specifically required by law, and the rules of the SEC, 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 such forward-looking statements.

You should read this prospectus, the registration statement of which this prospectus forms a part, the documents incorporated by reference herein, and any applicable prospectus supplement in their entirety and with the understanding that our actual future results may be materially different from those expressed in forward-looking statements.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of our common stock offered under this prospectus. Unless we indicate otherwise in the applicable prospectus supplement, we anticipate that any net proceeds will be used for working capital and general corporate purposes.

DESCRIPTION OF COMMON STOCK

The following is a summary of the material terms of our common stock, which is based upon, and is qualified in its entirety by reference to, our Articles of Incorporation, as amended (the "Articles of Incorporation"), our Amended and Restated Bylaws (the "Bylaws") and applicable provisions of the Virginia Stock Corporation Act ("VSCA"). This summary may not contain all the information that is important to you; you can obtain additional information regarding our Articles of Incorporation and Bylaws by referring to such documents, copies of which are included as exhibits to the registration statement of which this prospectus forms a part.

General

Under our Articles of Incorporation, we have authority to issue 500,000,000 shares of common stock, par value \$0.01 per share. As of May 17, 2017, there were 62,166,716 shares of common stock issued and outstanding. All shares of common stock will, when issued pursuant to this prospectus, be duly authorized, fully paid and nonassessable.

Dividend Rights

Subject to the rights of the holders of any of our preferred stock then outstanding, the holders of our common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. As of the date of this prospectus, we have not declared or paid any dividends on our shares of common stock, and there were no shares of preferred stock outstanding, although our board of directors is authorized to issue preferred stock with rights senior to those of the common stock without any further vote or action by the holders of our common stock.

Rights Upon Liquidation

In the event we are liquidated, dissolved or our affairs are wound up, after we pay or make adequate provision for all of our known debts and liabilities, each holder of common stock will receive distributions pro rata out of assets that we can legally use to pay distributions, subject to the rights of the holders of any of our preferred stock then outstanding.

Voting Rights

Holders of our common stock are entitled to one vote per share and will have the exclusive power to vote on all matters presented to our shareholders, including the election of directors, except as otherwise provided by the VSCA and subject to the rights of the holders of any of our preferred stock then outstanding. An election of directors by our shareholders will be determined by a plurality of the votes cast by the shareholders entitled to vote on the election, although we have recently adopted a director resignation policy applicable to director nominees in uncontested elections. Our Articles of Incorporation do not provide for cumulative voting. In accordance with our Articles of Incorporation, our board is divided into three classes serving staggered three-year terms, with one class being elected each year at our annual meeting of shareholders.

Subject to certain exceptions set forth in the VSCA, matters other than the election of directors generally will be approved if the votes cast by our shareholders favoring the action exceed the votes cast opposing the action. Subject to the rights of the holders of any of our preferred stock then outstanding, however, the affirmative vote of at least 75% of the voting power of the outstanding shares of our capital stock entitled to vote generally in the election of directors, voting together as a single group, will be required to take the following actions:

- remove a director, which may only be done for cause; and
- alter, amend, repeal, or adopt any provision inconsistent with, the provisions of (1) our Articles of Incorporation that provide for a classified board, director removal only for cause, filling of newly created or vacant directorships, or bylaw amendments or (2) our Bylaws.

Other Rights

Holders of our common stock will have no preference, appraisal or exchange rights, except for any appraisal rights provided by the VSCA. Furthermore, holders of our common stock have no conversion, sinking fund or redemption rights, or preemptive rights to subscribe for any of our securities.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Broadridge Investor Communication Solutions, Inc. Its address is 1717 Arch Street, Suite 1300, Philadelphia, PA 19103.

Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "INSM."

PLAN OF DISTRIBUTION

We may sell the common stock registered pursuant to this prospectus in the following ways:

- to or through underwriters;
- to or through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of the foregoing methods.

We reserve the right to sell directly to or exchange our common stock directly with investors on our own behalf in those jurisdictions where we are authorized to do so.

We may distribute such common stock from time to time in one or more transactions:

- at a fixed price or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We, or the purchasers of the common stock for whom the underwriters may act as agents, may compensate underwriters in the form of underwriting discounts or commissions, in connection with the sale of the common stock. Underwriters may sell our common stock to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for whom they may act as agents. Unless otherwise indicated in the applicable prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase our common stock as a principal and may then resell such common stock at varying prices to be determined by the dealer.

We will name any underwriter, dealer or agent involved in the offer and sale of common stock in the applicable prospectus supplement. In addition, we will describe in the applicable prospectus supplement the public offering or purchase price and the proceeds we will receive from the sale of our common stock, any compensation we will pay to underwriters, dealers or agents in connection with such offering of our common stock, any discounts, concessions or commissions allowed or re-allowed by underwriters to participating dealers, and any exchanges on which our common stock will be listed. Dealers and agents participating in the distribution of the common stock may be deemed to be underwriters, and any discounts and commissions received by them and any profit realized by them on resale of the common stock may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against certain civil liabilities, including liabilities under the Securities Act, and to reimburse these persons for certain expenses. We may also agree to contribute to payments that the underwriters, dealers or agents or any of their controlling persons may be required to make in respect of such liabilities. We may grant underwriters who participate in the distribution of the common stock we are registering pursuant to this prospectus an option to purchase additional shares in connection with a subsequent distribution. Certain underwriters, dealers or agents and their associates may engage in transactions with and perform services for us in the ordinary course of our business.

To facilitate the offering of our common stock, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock. Such transactions may include over-allotments or short sales of our common stock, which involve the sale by persons participating in the offering of more common stock than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their option to purchase additional shares, if any. In addition, these persons may stabilize or maintain the price of our common stock by bidding for or purchasing such common stock in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the common stock sold by them is repurchased in connection with stabilization transactions. Should these transactions be undertaken, they may be discontinued at any time.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the common stock being offered by this prospectus will be passed upon for us by Covington & Burling LLP, Washington, D.C. and/or Hunton & Williams LLP, Richmond, Virginia.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, and the effectiveness of our internal control over financial reporting as of December 31, 2016, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the Public Reference Room. Our SEC filings are also available to the public from the SEC's website at www.sec.gov. We maintain a website at www.insmed.com. The information contained in, or that can be accessed through, our website is not part of this prospectus. We have filed with the SEC a registration statement under the Securities Act with respect to the common stock registered pursuant hereto. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. For further information with respect to us and the common stock registered pursuant to this prospectus, you should review the registration statement, the applicable prospectus supplement, the information incorporated herein and therein, and the exhibits included herein and therein.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring to those publicly available documents. The information that we incorporate by reference is considered to be part of this prospectus. We incorporate by reference the documents listed below (File No. 000-30739) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of this registration statement and, in the case of any particular offering of our common stock, the date such offering is terminated:

- Annual Report on Form 10-K for the year ended December 31, 2016;
- Quarterly Report on Form 10-Q for the quarter ended March 31, 2017;
- Current Report on Form 8-K, filed with the SEC on May 19, 2017; and
- Description of our common stock contained in our registration statement on Form 8-A, dated June 1, 2000, including any amendment or report subsequently filed for the purpose of updating such description.

Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and information that we subsequently file with the SEC will automatically update and supersede the information herein to the extent inconsistent herewith. This means that it is important to review all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference has been modified or superseded.

You may request a copy of our SEC filings at no cost, by telephoning or writing us at the following telephone number or address:

Insmed Incorporated
10 Finderne Avenue, Building 10
Bridgewater, New Jersey 08807
Attention: Christine Pellizzari, General Counsel and Corporate Secretary
(908) 977-9900

\$250,000,000

Common Stock



Joint Book-Running Managers

Goldman Sachs & Co. LLC

Leerink Partners

Passive Book-Runner

Evercore ISI

Co-Lead Manager

Stifel
