INSMED INC

FORM 10-Q
(Quarterly Report)

Filed 11/02/17 for the Period Ending 09/30/17

Address	10 FINDERNE AVENUE BUILDING 10 BRIDGEWATER, NJ, 08807
Telephone	908-977-9900
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Industry	Biotechnology & Medical Research
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended September 30, 2017

OR

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

For the transition period from to

Commission File Number 0-30739

INSMED INCORPORATED

(Exact name of registrant as specified in its charter)

Virginia	**54-1972729**
(State or other jurisdiction of incorporation or organization)	(I.R.S. employer identification no.)
10 Finderne Avenue, Building 10 **Bridgewater, New Jersey**	**08807**
(Address of principal executive offices)	(Zip Code)

(908) 977-9900
(Registrant's telephone number including area code)

Not Applicable
(Former name, former address and former fiscal year, if changed since last report)

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

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

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

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

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

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

As of October 31, 2017 , there were 76,591,009 shares of the registrant's common stock, $0.01 par value, outstanding.

INSMED INCORPORATED
FORM 10-Q
FOR THE QUARTER ENDED SEPTEMBER 30, 2017

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Unless the context otherwise indicates, references in this Form 10-Q to "Insmed Incorporated" refers to Insmed Incorporated, a Virginia corporation, and "Company," "Insmed," "we," "us" and "our" refer to Insmed Incorporated together with its consolidated subsidiaries. INSMED and CONVERT are trademarks of Insmed Incorporated. This Form 10-Q also contains trademarks of third parties. Each trademark of another company appearing in this Form 10-Q is the property of its owner.

PART I. FINANCIAL INFORMATION

ITEM 1. CONSOLIDATED FINANCIAL STATEMENTS

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

	As of September 30, 2017 (unaudited)	As of December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 430,678	$ 162,591
Prepaid expenses and other current assets	6,802	5,816
Total current assets	437,480	168,407
In-process research and development	58,200	58,200
Fixed assets, net	8,975	10,020
Other assets	1,551	1,329
Total assets	$ 506,206	$ 237,956
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	$ 9,348	$ 10,439
Accrued expenses	18,802	16,822
Other current liabilities	616	728
Total current liabilities	28,766	27,989
Debt, long-term	55,388	54,791
Other long-term liabilities	747	693
Total liabilities	84,901	83,473
Shareholders' equity:		
Common stock, $0.01 par value; 500,000,000 authorized shares, 76,568,368 and 62,019,889 issued and outstanding shares at September 30, 2017 and December 31, 2016, respectively	766	620
Additional paid-in capital	1,313,006	919,164
Accumulated deficit	(892,501)	(765,236)
Accumulated other comprehensive income (loss)	34	(65)
Total shareholders' equity	421,305	154,483
Total liabilities and shareholders' equity	$ 506,206	$ 237,956

See accompanying notes to consolidated financial statements

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Revenues	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	26,675	23,433	75,800	67,851
General and administrative	17,408	13,716	47,767	38,498
Total operating expenses	44,083	37,149	123,567	106,349
Operating loss	(44,083)	(37,149)	(123,567)	(106,349)
Investment income	326	138	649	472
Interest expense	(1,496)	(769)	(4,459)	(2,015)
Other income, net	101	45	206	92
Loss before income taxes	(45,152)	(37,735)	(127,171)	(107,800)
Provision for income taxes	27	25	94	71
Net loss	$ (45,179)	$ (37,760)	$ (127,265)	$ (107,871)
Basic and diluted net loss per share	$ (0.69)	$ (0.61)	$ (2.01)	$ (1.74)
Weighted average basic and diluted common shares outstanding	65,312	61,878	63,199	61,871
Net loss	$ (45,179)	$ (37,760)	$ (127,265)	$ (107,871)
Other comprehensive income (loss):				
Foreign currency translation gains (losses)	76	(17)	99	(5)
Total comprehensive loss	$ (45,103)	$ (37,777)	$ (127,166)	$ (107,876)

See accompanying notes to consolidated financial statements

INSMED INCORPORATED
Consolidated Statements of Cash Flows (unaudited)
(in thousands)

	Nine Months Ended September 30,	
	2017	**2016**
Operating activities		
Net loss	$ (127,265)	$ (107,871)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	2,168	1,756
Stock-based compensation expense	13,332	13,879
Amortization of debt issuance costs	91	250
Accretion of back-end fee on debt	506	—
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(1,052)	(230)
Accounts payable	(921)	361
Accrued expenses and other	1,745	3,109
Net cash used in operating activities	(111,396)	(88,746)
Investing activities		
Purchase of fixed assets	(1,301)	(3,428)
Net cash used in investing activities	(1,301)	(3,428)
Financing activities		
Proceeds from exercise of stock options	2,953	128
Proceeds from issuance of debt	—	10,000
Payment of debt issuance costs	—	(308)
Proceeds from issuance of common stock, net	377,703	—
Net cash provided by financing activities	380,656	9,820
Effect of exchange rates on cash and cash equivalents	128	(4)
Net increase (decrease) in cash and cash equivalents	268,087	(82,358)
Cash and cash equivalents at beginning of period	162,591	282,876
Cash and cash equivalents at end of period	$ 430,678	$ 200,518
Supplemental disclosures of cash flow information:		
Cash paid for interest	$ 3,876	$ 2,471
Cash paid for income taxes	$ 62	$ 49

See accompanying notes to consolidated financial statements

INSMED INCORPORATED
NOTES TO UNAUDITED CONSOLIDATED FINANCIAL STATEMENTS

1. The Company and Basis of Presentation

Insmed is a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. The Company's lead product candidate is amikacin liposome inhalation suspension (ALIS) (formerly known as liposomal amikacin for inhalation, or LAI), 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. The Company's earlier clinical-stage pipeline includes INS1007 and INS1009. INS1007 is a novel oral, reversible inhibitor of dipeptidyl peptidase 1 (DPP1), 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).

The Company was incorporated in the Commonwealth of Virginia on November 29, 1999 and its principal executive offices are in Bridgewater, New Jersey. The Company has legal entities in the United States (US), Ireland, Germany, France, the United Kingdom (UK) and the Netherlands. All intercompany transactions and balances have been eliminated in consolidation.

The accompanying unaudited interim consolidated financial statements have been prepared pursuant to the rules and regulations for reporting on Form 10-Q. Accordingly, certain information and disclosures required by accounting principles generally accepted in the US for complete consolidated financial statements are not included herein. The unaudited interim consolidated financial statements should be read in conjunction with the audited consolidated financial statements and notes thereto included in the Company’s Annual Report on Form 10-K for the year ended December 31, 2016 .

The results of operations of any interim period are not necessarily indicative of the results of operations for the full year. The unaudited interim consolidated financial information presented herein reflects all normal adjustments that are, in the opinion of management, necessary for a fair statement of the financial position, results of operations and cash flows for the periods presented.

2. Summary of Significant Accounting Policies

The following are interim updates to certain of the policies described in “Note 2” to the Company’s audited consolidated financial statements in the Company’s Annual Report on Form 10-K for the year ended December 31, 2016 :

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

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

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

The Company's only financial assets and liabilities which were measured at fair value as of September 30, 2017 and December 31, 2016 were Level 1 and such assets were comprised of cash and cash equivalents of $430.7 million and $162.6 million , respectively.

The Company's cash and cash equivalents permit daily redemption and the fair values of these investments are based upon the quoted prices in active markets provided by the holding financial institutions. Cash equivalents consist of liquid investments with a maturity of three months or less from the date of purchase.

The Company recognizes transfers between levels within the fair value hierarchy, if any, at the end of each quarter. There were no transfers in or out of Level 1, Level 2 or Level 3 during the three and nine months ended September 30, 2017 and 2016 , respectively.

As of September 30, 2017 and December 31, 2016 , the Company held no securities that were in an unrealized gain or loss position. The Company reviews the status of each security quarterly to determine whether an other-than-temporary impairment has occurred. In making its determination, the Company considers a number of factors, including: (1) the significance of the decline; (2) whether the securities were rated below investment grade; (3) how long the securities have been in an unrealized loss position; and (4) the Company's ability and intent to retain the investment for a sufficient period of time for it to recover.

Net Loss Per Share - Basic net loss per share is computed by dividing net loss by the weighted average number of common shares outstanding during the period. Diluted net loss per share is computed by dividing net loss by the weighted average number of common shares and other dilutive securities outstanding during the period. Potentially dilutive securities from stock options and restricted stock units (RSUs) would be anti-dilutive as the Company incurred a net loss. Potentially dilutive common shares resulting from the assumed exercise of outstanding stock options are determined based on the treasury stock method.

The following table sets forth the reconciliation of the weighted average number of common shares used to compute basic and diluted net loss per share for the three and nine months ended September 30, 2017 and 2016 :

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
	(in thousands, except per share amounts)			
Numerator:				
Net loss	$ (45,179)	$ (37,760)	$ (127,265)	$ (107,871)
Denominator:				
Weighted average common shares used in calculation of basic net loss per share:	65,312	61,878	63,199	61,871
Effect of dilutive securities:				
Common stock options	—	—	—	—
RSUs	—	—	—	—
Weighted average common shares outstanding used in calculation of diluted net loss per share	65,312	61,878	63,199	61,871
Net loss per share:				
Basic and Diluted	$ (0.69)	$ (0.61)	$ (2.01)	$ (1.74)

The following potentially dilutive securities have been excluded from the computations of diluted weighted average common shares outstanding as of September 30, 2017 and 2016 as their effect would have been anti-dilutive (in thousands):

	2017	2016
Stock options to purchase common stock	8,601	7,306
Unvested RSUs	47	89

Recently Adopted Accounting Pronouncements - In August 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2014-15, *Presentation of Financial Statements—Going Concern (Subtopic*

205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern , which defines management's responsibility to perform interim and annual assessments of an entity's ability to continue as a going concern, and to provide related footnote disclosures if there is substantial doubt about its ability to continue as a going concern. The new standard was effective for the annual period ending after December 15, 2016, and for interim periods thereafter. The Company adopted ASU 2014-15 in the fourth quarter of 2016 , which had no impact on the Company's consolidated financial statements. The interim assessment during the first three quarters of 2017 did not have an impact on the consolidated financial statements.

The Company had $430.7 million in cash and cash equivalents as of September 30, 2017 and reported a net loss of $127.3 million for the nine months ended September 30, 2017 . Historically, the Company has funded its operations through public offerings of equity securities and debt financings. To date, the Company has not generated material revenue from ALIS. The Company does not expect to generate material revenue unless or until marketing approval is received for ALIS. Accordingly, the Company expects to continue to incur losses while funding research and development (R&D) activities, regulatory submissions, potential commercial launch activities and general and administrative expenses. The Company expects its future cash requirements to be substantial, and the Company will need to raise additional capital to fund operations, to develop and commercialize ALIS, to develop INS1007 and INS1009 and to develop, acquire, in-license or co-promote other products that address orphan or rare diseases.

ASU 2014-15 requires the Company to evaluate whether it has sufficient resources to fund operations for the next 12 months from the filing date without regard to whether or not it can raise capital in the future. The Company believes it currently has sufficient funds to meet its financial needs for at least the next 12 months. In September 2017, the Company completed an underwritten offering of 14.1 million shares of its common stock for cash proceeds of $377.7 million , net of fees and expenses related to the offering. The Company will be opportunistic in raising additional capital within the next 12 months and may do so through equity or debt financing(s), strategic transactions or otherwise. The source, timing and availability of any future financing or other transaction will depend principally upon continued progress in the Company's regulatory, development and pre-commercial activities. Any equity or debt financing will also be contingent upon equity and debt market conditions and interest rates at the time. If the Company is unable to obtain sufficient additional funds when required, the Company may be forced to delay, restrict or eliminate all or a portion of its R&D programs, pre-commercialization activities, or dispose of assets or technology.

In March 2016, the FASB issued ASU 2016-9, *Improvements to Employee Share-Based Payment Accounting* , which amends Accounting Standards Codification (ASC) Topic 718, *Compensation—Stock Compensation* . ASU 2016-9 simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. ASU 2016-9 was effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years. The Company adopted ASU 2016-9 in the first quarter of 2017. The impact of the adoption was not material to the consolidated financial statements.

3. Identifiable Intangible Asset

The Company believes there are no indicators of impairment relating to its in-process research and development intangible asset as of September 30, 2017 .

4. Accrued Expenses

Accrued expenses consist of the following:

	As of September 30, 2017	As of December 31, 2016
	(in thousands)	
Accrued clinical trial expenses	$ 8,560	$ 7,071
Accrued compensation	6,634	6,937
Accrued professional fees	2,057	1,604
Accrued technical operation expenses	742	591
Accrued interest payable	424	438
Other accrued expenses	385	181
	$ 18,802	$ 16,822

5. Debt

On September 30, 2016, the Company and its domestic subsidiaries, as co-borrowers, entered into an Amended and Restated Loan and Security Agreement (the A&R Loan Agreement) with Hercules Capital, Inc. (Hercules). The A&R Loan Agreement included a total commitment from Hercules of up to $55.0 million , of which $25.0 million was previously outstanding. The amount of borrowings was increased by $10.0 million to an aggregate total of $35.0 million on September 30, 2016. An additional $20.0 million was available at the Company's option through June 30, 2017 subject to certain conditions, including the payment of a facility fee of 0.375% . The Company exercised this option in early October 2016 and borrowed an additional $20.0 million in connection with its upfront payment obligation under the license agreement with AstraZeneca AB. The interest rate for the term is floating and is calculated as the greater of (i) 9.25% or (ii) 9.25% plus the sum of the US prime rate minus 4.50% , along with a backend fee of 4.15% of the aggregate principal amount outstanding and an aggregate facility fee of $337,500 . The maturity date of the loan facility was also extended to October 1, 2020. In connection with the Company generating and announcing top-line data from the CONVERT study on September 5, 2017 that supports the filing of a New Drug Application (NDA), along with the completion of the equity financing, the interest-only period was automatically extended through May 1, 2019 and the Company's requirement to have a consolidated minimum cash liquidity in an amount no less than $25.0 million was eliminated. In addition, pursuant to the A&R Loan Agreement, Hercules has the right to participate, in an aggregate amount of up to $2.0 million , in a subsequent private financing that involves the issuance of our equity securities.

In connection with the A&R Loan Agreement, the Company granted Hercules a first position lien on all of the Company's assets, excluding intellectual property. Prepayment of the loans made pursuant to the A&R Loan Agreement is subject to penalty. The back-end fee of 4.15% on the aggregate outstanding principal balance is being charged to interest expense (and accreted to the debt) using the effective interest method over the life of the A&R Loan Agreement. Debt issuance fees paid to Hercules were recorded as a discount on the debt and are being amortized to interest expense using the effective interest method over the life of the A&R Loan Agreement.

The following table presents the components of the Company's debt balance as of September 30, 2017 (in thousands):

Notes payable	$	55,000
Accretion of back-end fee on debt		677
Debt issuance costs, unamortized		(289)
Debt, long-term	$	55,388

As of September 30, 2017 , future principal repayments of the debt for each of the fiscal years through maturity were as follows (in thousands):

Year Ending December 31:		
2017	$	—
2018		—
2019		13,399
2020		41,601
	$	55,000

The estimated fair value of the debt (categorized as a Level 2 liability for fair value measurement purposes) is determined using current market factors and the ability of the Company to obtain debt at comparable terms to those that are currently in place. The Company believes the estimated fair value at September 30, 2017 approximates the carrying amount.

6. Shareholders' Equity

Common Stock — As of September 30, 2017 , the Company had 500,000,000 shares of common stock authorized with a par value of $0.01 and 76,568,368 shares of common stock issued and outstanding. In addition, as of September 30, 2017 , the Company had reserved 8,601,293 shares of common stock for issuance upon the exercise of outstanding stock options and 46,914 shares of common stock for issuance upon the vesting of RSUs.

On September 6, 2017 , the Company completed an underwritten public offering of 14,123,150 shares of the Company's common stock, which included the underwriter's exercise in full of its over-allotment option of 1,842,150
shares, at a price to the public of $28.50 per share. The Company's net proceeds from the sale of the shares, after deducting the underwriter's discount and offering expenses of $24.8 million , were $ 377.7 million .

Preferred Stock — As of September 30, 2017 , the Company had 200,000,000 shares of preferred stock authorized with a par value of $0.01 and no shares of preferred stock were issued and outstanding.

7. Stock-Based Compensation

The Company's current equity compensation plan, the 2017 Incentive Plan, was approved by shareholders at the Company's Annual Meeting of Shareholders on May 18, 2017. The 2017 Incentive Plan is administered by the Compensation Committee and the Board of Directors of the Company. Under the terms of the 2017 Incentive Plan, the Company is authorized to grant a variety of incentive awards based on its common stock, including stock options (both incentive stock options and non-qualified stock options), RSUs, performance options/shares and other stock awards, as well as pay incentive bonuses to eligible employees and non-employee directors. On May 18, 2017, upon the approval of the 2017 Incentive Plan by shareholders, 5,000,000 shares were authorized for issuance thereunder, plus any shares subject to then-outstanding awards under the 2015 Incentive Plan and the 2013 Incentive Plan that subsequently were canceled, terminated unearned, expired, were forfeited, lapsed for any reason or were settled in cash without the delivery of shares. As of September 30, 2017 , 4,929,910 shares remained for future issuance under the 2017 Incentive Plan. The 2017 Incentive Plan will terminate on April 3, 2027 unless it is extended or terminated earlier pursuant to its terms. In addition, from time to time, the Company makes inducement grants of stock options. These awards are made pursuant to the NASDAQ inducement grant exception as a component of new hires' employment compensation in connection with the Company's equity grant program. During the nine months ended September 30, 2017 , the Company granted inducement stock options covering 236,370 shares of the Company's common stock to new employees.

Stock Options - The Company calculates the fair value of stock options granted using the Black-Scholes valuation model. The following table summarizes the Company's grant date fair value and assumptions used in determining the fair value of all stock options granted:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Volatility	72%-73%	75%-76%	72%-74%	75%-77%
Risk-free interest rate	1.73%-1.93%	1.00%-1.18%	1.73%-1.99%	1.00%-1.73%
Dividend yield	0.0%	0.0%	0.0%	0.0%
Expected option term (in years)	6.25	6.25	6.25	6.25
Weighted average fair value of stock options granted	$9.59	$7.79	$10.18	$8.74

For each period presented, the volatility factor was based on the Company's historical volatility during the expected option term. Estimated forfeitures are based on the actual percentage of option forfeitures since the closing of the Company's merger with Transave, Inc. in December 2010.

From time to time, the Company grants performance-condition options to certain of its employees. Vesting of these options is subject to the Company achieving certain performance criteria established at the date of grant and the grantees fulfilling a service condition (continued employment). As of September 30, 2017 , the Company had performance options totaling 133,334 shares outstanding which had not yet met the recognition criteria.

The following table summarizes the Company's aggregate stock option activity for the nine months ended September 30, 2017 :

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in thousands)
Options outstanding at December 31, 2016	7,116,706	$ 13.30		
Granted	2,207,390	$ 15.42		
Exercised	(336,135)	$ 8.78		
Forfeited or expired	(386,668)	$ 15.59		
Options outstanding at September 30, 2017	8,601,293	$ 13.92	7.65	$ 148,771
Vested and expected to vest at September 30, 2017	8,269,230	$ 13.88	7.60	$ 143,327
Exercisable at September 30, 2017	3,904,073	$ 12.46	6.40	$ 73,193

The total intrinsic value of stock options exercised during the three months ended September 30, 2017 and 2016 was $1.4 million and $0.0 million , respectively, and during the nine months ended September 30, 2017 and 2016 was $3.5 million and $0.1 million , respectively.

As of September 30, 2017 , there was $31.5 million of unrecognized compensation expense related to unvested stock options which is expected to be recognized over a weighted average period of 2.7 years. Included in unrecognized compensation expense was $1.1 million related to outstanding performance-condition options. The following table summarizes the range of exercise prices and the number of stock options outstanding and exercisable:

Outstanding as of September 30, 2017					Exercisable as of September 30, 2017	
Range of Exercise Prices ($)		Number of Options	Weighted Average Remaining Contractual Term (in years)	Weighted Average Exercise Price ($)	Number of Options	Weighted Average Exercise Price ($)
3.03	4.55	988,195	4.89	3.59	988,195	3.59
6.90	6.90	137,577	5.47	6.90	100,077	6.90
6.96	10.85	1,081,121	8.55	10.76	289,330	10.52
11.14	12.58	1,095,757	6.65	12.17	735,792	12.16
12.66	13.58	185,880	7.76	13.24	89,704	13.29
13.67	13.67	865,660	9.27	13.67	—	—
13.94	15.91	862,300	8.01	14.97	339,372	14.55
16.07	16.16	1,009,781	7.93	16.13	463,410	16.12
16.19	17.16	871,266	9.34	17.10	31,741	16.30
17.24	27.38	1,503,756	7.41	21.20	866,452	21.13

Restricted Stock and Restricted Stock Units — The Company may grant restricted stock (RS) and RSUs to eligible employees, including its executives, and non-employee directors. Each share of RS vests, and each RSU represents a right to receive one share of the Company's common stock, upon the completion of a specific period of continued service or achievement of a certain milestone. RS and RSU awards granted are valued at the market price of the Company's common stock on the date of grant. The Company recognizes noncash compensation expense for the fair values of these RS and RSUs on a straight-line basis over the requisite service period of these awards. The following table summarizes the Company's RSU award activity during the nine months ended September 30, 2017 :

	Number of RSUs	Weighted Average Grant Price ($)
Outstanding at December 31, 2016	89,194	10.85
Granted	46,914	17.16
Released	(89,194)	(10.85)
Outstanding at September 30, 2017	46,914	17.16

The following table summarizes the aggregate stock-based compensation recorded in the Consolidated Statements of Comprehensive Loss related to stock options and RSUs during the three and nine months ended September 30, 2017 and 2016 :

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
	(in millions)			
Research and development expenses	$ 1.8	$ 1.7	$ 4.8	$ 4.6
General and administrative expenses	2.9	3.4	8.5	9.3
Total	$ 4.7	$ 5.1	$ 13.3	$ 13.9

8. Income Taxes

The Company's provision for income taxes was $27,000 and $94,000 for the three and nine months ended September 30, 2017 , respectively, and $25,000 and $71,000 for the three and nine months ended September 30, 2016 , respectively. The provision for income taxes in all periods was a result of certain of the Company's subsidiaries in Europe, which had taxable income during the three and nine months ended September 30, 2017 and 2016 . In jurisdictions where the Company has net losses, there was a full valuation allowance recorded against the Company's deferred tax assets and therefore no tax benefit was recorded. The Company is subject to US federal, US state and foreign income taxes. The statute of limitations for tax audit is open for the Company's US federal tax returns for the years ended 2013 and later and is generally open for certain states for the years 2012 and later. The Company has incurred net operating losses since inception, except for 2009. Loss carryforwards are subject to audit in any tax year in which those losses are utilized, notwithstanding the year of origin. As of September 30, 2017 and December 31, 2016 , the Company had recorded no reserves for unrecognized income tax benefits, nor had it recorded any accrued interest or penalties related to uncertain tax positions. The Company does not anticipate any material changes in the amount of unrecognized tax positions over the next 12 months.

9. Commitments and Contingencies

The Company has an operating lease for office and laboratory space located in Bridgewater, NJ, its corporate headquarters, for which the initial lease term expires in November 2019. Future minimum rental payments under this lease are $2.2 million . In July 2016, the Company signed an operating lease for additional laboratory space located in Bridgewater, NJ for which the initial lease term expires in December 2021. Future minimum rental payments under this lease are $2.0 million .

Rent expense charged to operations was $0.4 million for both the three months ended September 30, 2017 and 2016 , and $1.1 million and $0.9 million for the nine months ended September 30, 2017 and 2016 , respectively. Future minimum rental payments required under the Company's operating leases for the period from October 1, 2017 to December 31, 2017 and for each of the five years thereafter are as follows (in thousands):

Year Ending December 31:	
2017 (remaining)	$ 377
2018	1,520
2019	1,421
2020	477
2021	498
2022	—
	$ 4,293

Purchase Commitments

In September 2017, the Company increased its purchase commitments made in the normal course of business with contract manufacturing organizations (CMOs) and various other suppliers related to the production requirements for ALIS. These purchase commitments have increased as a result of the release of top-line results from the CONVERT study.

Legal Proceedings

On July 15, 2016, a lawsuit captioned Hoey v. Insmed Incorporated, et al, No. 3:16-cv-04323-FLW-TJB (D.N.J. July 15, 2016) was filed in the US District Court for the District of New Jersey on behalf of a putative class of investors who purchased the Company's common stock from March 18, 2013 through June 8, 2016. The complaint alleged that the Company and certain of its executives violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 (Exchange Act) by misrepresenting and/or omitting the likelihood of the European Medicines Agency (EMA) approving the Company's European marketing authorization application (MAA) for use of ALIS in the treatment of NTM lung disease and the likelihood of commercialization of ALIS in Europe.

On October 25, 2016, the Court issued an order appointing Bucks County Employees Retirement Fund as lead plaintiff for the putative class. On December 15, 2016, the lead plaintiff filed an amended complaint that shortens the putative class period for the Exchange Act claims to March 26, 2014 through June 8, 2016 and adds claims under Sections 11, 12, and 15 of the Securities Act of 1933 (Securities Act) on behalf of a putative class of investors who purchased common stock in or traceable to the Company's March 31, 2015 public offering. The amended complaint names as defendants in the Securities Act claims the Company, certain directors and officers, and the investment banks who served as underwriters in connection with the secondary offering. The amended complaint alleges defendants violated the Securities Act by using a purportedly misleading definition of "culture conversion" and supposedly failing to disclose in the offering materials purported flaws in its Phase 2 study that made the secondary offering risky or speculative. The amended complaint seeks damages in an unspecified amount. The Company moved to dismiss the amended complaint on March 1, 2017. The lead plaintiff opposed the motion on May 17, 2017 and the Company provided its reply brief on July 11, 2017. On July 20, 2017, the plaintiff asked for leave to file a sur-reply in further opposition to the Company's motion to dismiss the amended complaint, which the Company has opposed. The Company believes that the allegations in the complaints are without merit and intends to defend the lawsuit vigorously; however, there can be no assurance regarding the ultimate outcome of the lawsuit.

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

10. Subsequent Event

In October 2017, the Company exercised an option to buy-down the future royalties that will be payable to PARI Pharma GmbH (PARI). Pursuant to the existing licensing agreement, PARI is entitled to receive royalty payments in the mid-single digits on the annual global net sales of ALIS, subject to certain specified annual minimum royalties. The royalty buy-down will enable the Company to reduce the royalty payments due to PARI based on the annual global net sales of ALIS. The payment to PARI will be included as a component of general and administrative expenses in the fourth quarter of 2017.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Cautionary Note Regarding Forward Looking Statements

This Quarterly Report on Form 10-Q contains 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 US 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 US 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;*
- *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; and*
- *lack of experience operating internationally.*

We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made. Any forward-looking statement is based on information current as of the date of this Quarterly Report on Form 10-Q and speaks only as of the date on which such statement is made. Actual events or results may differ materially from the results, plans, intentions or expectations anticipated in these forward-looking statements as a result of a variety of factors, many of which are beyond our control. More information on factors that could cause actual results to differ materially from those anticipated is included from time to time in our reports filed with the Securities and Exchange Commission (SEC), including, but not limited to, those described in the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in this Quarterly Report on Form 10-Q and our Annual Report on Form 10-K for the fiscal year ended December 31, 2016. 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 the forward-looking statements.

The following discussion should be read in conjunction with our consolidated financial statements and related notes thereto included elsewhere in this Quarterly Report on Form 10-Q and the consolidated financial statements and related notes thereto in our Annual Report on Form 10-K for the year ended December 31, 2016.

OVERVIEW

We are 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, or LAI), 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 can be fatal. Our earlier clinical-stage pipeline includes INS1007 and INS1009. INS1007 is a novel oral, reversible inhibitor of dipeptidyl peptidase 1 (DPP1), 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).

The table below summarizes the current status and anticipated milestones for our principal product candidates: ALIS, INS1007, and INS1009.

Product Candidate/Target Indications	Status	Next Expected Milestones
ALIS for NTM lung infections	• We announced top-line data for the CONVERT study on September 5, 2017. Based on top-line results, the CONVERT study met its primary endpoint of culture conversion, which we define as three consecutive negative monthly sputum cultures by month six with statistical and clinical significance, with 29% of patients in the ALIS plus current guidelines-based therapy (GBT) arm achieving culture conversion, compared to 9% of patients in the GBT-only arm ($p<0.0001$). • The CONVERT study is a randomized, open-label global phase 3 clinical study of ALIS in adult patients with treatment refractory NTM lung disease caused by MAC. • The FDA has designated ALIS as an orphan drug, a breakthrough therapy, and a qualified infectious disease product (QIDP). • The European Commission has granted an orphan designation for ALIS for the treatment of NTM lung disease.	• We plan to pursue accelerated approval for ALIS in the US based on data from the CONVERT study. We intend to seek marketing approvals for ALIS in certain countries outside the US, when sufficient data are available. If approved, we expect ALIS would be the first inhaled antibiotic specifically indicated for the treatment of NTM lung disease caused by MAC in North America, Japan and Europe. • If approved, we plan to commercialize ALIS in the US, Japan, certain countries in Europe, and certain other countries.
INS1007 (oral reversible inhibitor of DPP1) for non-CF bronchiectasis and other rare diseases	• We are in preparations for the WILLOW study, a global phase 2, randomized, double-blind, placebo-controlled, parallel-group, multi-center clinical study to assess the efficacy, safety and tolerability, and pharmacokinetics of INS1007 administered once daily for 24 weeks in subjects with non-CF bronchiectasis. • We are currently assessing our regulatory strategies with regard to orphan drug designation and other pathways that could expedite the development and regulatory reviews of INS1007 in the US and the EU.	• We have received a "study may proceed letter" from the FDA and expect to commence enrollment in the WILLOW clinical study of INS1007 in the fourth quarter of 2017. • We are exploring the potential of INS1007 in various neutrophil-driven inflammatory conditions.
INS1009 (inhaled nanoparticle formulation of a treprostinil prodrug) for rare pulmonary disorders	• The results of our phase 1 study of INS1009 were presented at the European Respiratory Society international congress in September 2016. • The phase 1 study was a randomized, double-blind, placebo-controlled, single ascending dose study of INS1009 for inhalation to determine its safety, tolerability, and pharmacokinetics in healthy volunteers.	• We believe INS1009 may offer a differentiated product profile for rare pulmonary disorders, including PAH, and we are currently evaluating our options to advance its development including exploring its use as an inhaled dry powder formulation.

Our earlier-stage pipeline includes preclinical compounds that we are evaluating in multiple rare diseases of unmet medical need, including methicillin-resistant staph aureus (MRSA) and NTM. To complement our internal research and development, we actively evaluate in-licensing and acquisition opportunities for a broad range of rare diseases.

Our Strategy

Our strategy focuses on the needs of patients with rare diseases. We are currently primarily focused on the development and commercialization of ALIS. We are not aware of any approved inhaled therapies specifically indicated to treat NTM lung disease in North America, Japan or Europe. While we believe that ALIS has the potential to treat a number of different bacterial infections, we are prioritizing securing US regulatory approval of ALIS for adult patients with NTM lung disease caused by MAC. We are also advancing earlier-stage programs in other rare pulmonary disorders.

Our current priorities are as follows:

- Completing the CONVERT study;
- Preparing a New Drug Application (NDA) for submission under subpart H to the FDA for ALIS based on the primary endpoint of the CONVERT study;
- Ensuring our product supply chain will support the commercialization, if approved, and future life cycle management programs of ALIS;
- Preparing for potential commercialization of ALIS in the US, Japan, certain countries in Europe, and certain other countries;
- Developing the core value dossier to support the global reimbursement of ALIS;
- Supporting further research and lifecycle management strategies for ALIS, including exploring the potential use of ALIS as part of a front-line, multi-drug regimen and as maintenance monotherapy to prevent recurrence (defined as true relapse or reinfection) of NTM lung disease;
- Starting enrollment of the WILLOW phase 2 study of INS1007 in non-CF bronchiectasis;
- Generating preclinical findings from our earlier-stage program(s); and
- Expanding our rare disease pipeline through corporate development.

Product Pipeline

ALIS for Patients with NTM Lung Disease

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

The FDA has designated ALIS as an orphan drug, a breakthrough therapy, and a QIDP for NTM lung disease. Orphan designation features seven years of post-approval marketing exclusivity in the approved indication, and QIDP features an additional five years of post-approval exclusivity in the approved indication. As a result, ALIS would have 12 years of post-approval marketing exclusivity in the US, if approved. A QIDP-designated product is eligible for fast track status and is often granted priority review status. A priority review designation for a drug means the FDA's goal is to take action on the NDA within six months following the filing date, as compared to within 10 months following the filing date under a standard review.

The CONVERT Study and 312 Study

CONVERT Top-Line Efficacy Data

We announced top-line data for the CONVERT study on September 5, 2017. The CONVERT study enrolled 336 adult patients with NTM lung disease caused by MAC who were refractory to at least six months of treatment on current GBT of a multi-drug regimen. 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 six. 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.

The protocol for the CONVERT study incorporates feedback from the FDA and the EMA via its scientific advice working party process, as well as local health authorities in other countries, including Japan's Pharmaceuticals and Medical Devices Agency (PMDA). Because the CONVERT study met the primary endpoint of culture conversion by month six based on the top-line results, we plan to submit an NDA pursuant to 21 C.F.R. Part 314 Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) (Subpart H), which permits the FDA to approve a product candidate based on a surrogate or intermediate endpoint, provided (i) we commit to study the product candidate further to verify and describe the confirmatory data of its clinical benefit and (ii) the FDA concurs with other aspects of the NDA. We believe that efficacy data from the CONVERT study after month six in combination with the durability data, if successful, will suffice to meet both the accelerated and confirmatory data requirements. We expect that full approval would be contingent on FDA review of, among other things, the final analyses of sustainability and durability of culture conversion for converters.

CONVERT Top-Line Safety and Tolerability Data

Approximately 98% of patients in the ALIS plus GBT arm of the study experienced at least one treatment-emergent adverse event (TEAE), compared to 91% 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% and 18% 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.

		2:1 Randomization	
Patients Reporting STEAEs >3% in Either Arm		**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%, with an 8.9% dropout rate in the GBT-only arm and a 19.6% dropout rate in the ALIS plus GBT arm.

CONVERT Extension Study (or 312 Study)

All non-converters in the CONVERT study, as determined at the month eight visit, may be eligible to enter a separate 12-month, single-arm, open-label study (the 312 study). The primary objective of the 312 study is to evaluate the long-term safety and tolerability of ALIS in combination with a standard multi-drug regimen. The secondary endpoints of the 312 study include evaluating the proportion of patients achieving culture conversion (three consecutive monthly negative sputum cultures) by month six and the proportion of patients achieving culture conversion by month 12 (end of treatment).

Phase 2 Study (or 112 Study)

Our completed phase 2 study (or 112 study) was a randomized, double-blind, placebo-controlled study that evaluated the efficacy and safety of ALIS in adults with NTM lung disease due to MAC or *M. abscessus* that was refractory to guideline-based therapy. In October 2016, the results from the phase 2 study were published online in the *American Journal of Respiratory and Critical Care Medicine* (Olivier et al. 2016).

The study included an 84-day double-blind phase in which patients were randomized 1:1 either to ALIS once-daily plus a multi-drug regimen or to placebo once-daily plus a multi-drug regimen. After completing the 84-day double-blind phase, patients had the option of continuing in an 84-day open-label phase during which all patients received ALIS plus the same multi-drug regimen. The study also included 28-day and 12-month off-ALIS follow-up assessments. Eighty-nine (89) patients were randomized and dosed in the study. Of the 80 patients who completed the 84-day double-blind phase, 78 patients entered the open-label phase and received ALIS plus the same multi-drug regimen for an additional 84 days. Seventy-six (76) percent (59/78) of patients who entered the open-label phase of the study completed the open-label study.

The primary efficacy endpoint of the study was the change from baseline (Day 1) to the end of the double-blind phase of the trial (Day 84) in a semi-quantitative measurement of mycobacterial density on a seven-point scale. ALIS did not meet the pre-specified level for statistical significance although there was a positive trend ($p=0.072$) in favor of ALIS. The p-value for the key secondary endpoint of culture conversion to negative at Day 84 was 0.003, in favor of ALIS. A shorter time to first negative sputum culture was also observed with ALIS relative to placebo during the double-blind phase ($p=0.013$).

The microbiologic outcomes from the 112 study were also explored post hoc using a more stringent definition of culture conversion, which was defined as at least three consecutive monthly sputum samples that test negative for NTM, consistent with the definition of culture conversion in the guidelines and in clinical practice. Twenty-three (23) patients achieved at least three consecutive negative monthly sputum samples by the 28-day follow-up assessment, of which four started to convert at baseline prior to administration of study drug. For the other 19 patients who achieved culture conversion, 17 achieved culture conversion after receiving ALIS (10 during the double-blind phase and seven after entering the open-label phase, of which six received ALIS for the first time in the open-label phase). Two patients achieved culture conversion while receiving placebo during the double-blind phase. The majority of patients who achieved culture conversion (three consecutive negative monthly sputum samples) during the double-blind phase continued to have negative cultures through the open-label and follow-up phases.

At the end of the double-blind phase, the ALIS group improved from baseline in mean distance walked in the six-minute walk test. At the end of the open-label phase, patients in the ALIS group continued to improve in the mean distance walked in the six-minute walk test, while the patients who previously received placebo in the double-blind phase and subsequently received ALIS in the open-label phase demonstrated a reduced rate of decline from baseline.

Approximately 90% of patients in both treatment groups experienced at least one treatment-emergent adverse event, with most events either mild or moderate in severity. During the double-blind phase a greater percentage of patients treated with ALIS experienced, among others, dysphonia, bronchiectasis exacerbation, cough, oropharyngeal pain, fatigue, chest discomfort, wheezing, and infective pulmonary exacerbation of cystic fibrosis (CF). No clinically relevant changes were detected in laboratory values and vital signs.

Further Research and Lifecycle Management for ALIS

We are currently exploring and supporting research and lifecycle management programs for ALIS beyond refractory NTM lung infections caused by MAC. Specifically, we are evaluating future study designs focusing on the MAC disease treatment pathway, including front-line treatment and monotherapy maintenance to prevent recurrence (defined as true relapse or reinfection) of NTM lung disease. If the data from the CONVERT study are sufficient to support our MAAs and regulatory bodies approve ALIS, such lifecycle management studies could enable us to reach more potential patients. These initiatives

may include new clinical studies sponsored by us or investigator-initiated studies, which are clinical studies initiated and sponsored by physicians or research institutions with funding from us.

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 US, 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 US, 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	40,000-50,000	10,000-15,000
Japan	125,000-145,000	60,000-70,000	15,000-18,000
EU5	14,000	4,400	1,400

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 US and internationally.

NTM Lung Disease Market Opportunity in Japan

We are currently exploring the NTM market opportunity for ALIS in Japan. If the data from the CONVERT study are sufficient to support our MAAs, and the FDA approves ALIS, we expect our first regulatory filing after the US to be in Japan. We plan to establish a presence in Japan in 2018, including hiring local employees to closely manage our regulatory and pre-commercial activities.

Under the Japanese regulatory system administered by the PMDA, pre-marketing approval and clinical studies are required for all pharmaceutical products. To obtain manufacturing/marketing approval, a Company must submit an application for approval to the MHLW with results of nonclinical and clinical studies to show the quality, efficacy and safety of a new product candidate. A data compliance review, on-site inspection for good clinical practice, audit and detailed data review for compliance with current good manufacturing practices are undertaken by the PMDA. The application is then discussed by the committees of the Pharmaceutical Affairs and Food Sanitation Council. Based on the results of these reviews, the final decision on approval is made by MHLW. In Japan, the National Health Insurance system maintains a Drug Price List specifying which pharmaceutical products are eligible for reimbursement, and the MHLW sets the prices of the products on this list. After receipt of marketing approval, negotiations regarding the reimbursement price with MHLW would begin. Price would be determined within 60 to 90 days unless the applicant disagrees, which may result in extended pricing negotiations. The government generally introduces price cut rounds every other year and also mandates price decreases for specific products. New products judged innovative or useful, that are indicated for pediatric use, or that target orphan or small population diseases, however, may be eligible for a pricing premium. The government has also promoted the use of generics, where available.

INS1007

INS1007 is a small molecule, oral, reversible inhibitor of DPP1, which we in-licensed from AstraZeneca in October 2016. DPP1 is an enzyme responsible for activating neutrophil serine proteases in neutrophils when they are formed in the bone marrow. Neutrophils are the most common type of white blood cell and play an essential role in pathogen destruction and inflammatory mediation. Neutrophils contain the neutrophil serine proteases, neutrophil elastase, proteinase 3, and cathepsin G, that have been implicated in a variety of inflammatory diseases. In chronic inflammatory lung diseases,

neutrophils accumulate in the airways and release active neutrophil serine proteases in excess that cause lung destruction and inflammation. INS1007 may decrease the damaging effects of inflammatory diseases, such as non-CF bronchiectasis, by inhibiting DPP1 and its activation of neutrophil serine proteases. Non-CF bronchiectasis is a progressive pulmonary disorder in which the bronchi become permanently dilated due to chronic inflammation and infection. Currently, there is no cure, and we are not aware of any approved therapies for non-CF bronchiectasis.

The WILLOW Study

We are in preparations for the WILLOW study, a global phase 2, randomized, double-blind, placebo-controlled, parallel group, multi-center clinical study to assess the efficacy, safety and tolerability, and pharmacokinetics of INS1007 administered once daily for 24 weeks in subjects with non-CF bronchiectasis. We have received a "study may proceed letter" from the FDA and expect to commence enrollment in the study in the fourth quarter of 2017. In addition, we are exploring the potential of INS1007 in various neutrophil-driven inflammatory conditions.

Phase 1 Study Results

In a phase 1 study of healthy volunteers conducted by AstraZeneca, INS1007 (previously AZD7986) was well tolerated and demonstrated inhibition of the activity of the neutrophil serine protease neutrophil elastase in a dose and concentration dependent manner. In preclinical studies, it was shown to reversibly inhibit DPP1 and the activation of neutrophil serine proteases within maturing neutrophils.

INS1009

INS1009 is an investigational sustained-release inhaled treprostinil prodrug nanoparticle formulation that has the potential to address certain of the current limitations of existing prostanoid therapies. We believe that INS1009 prolongs duration of effect and may provide PAH patients with greater consistency in pulmonary arterial pressure reduction over time. Current inhaled prostanoid therapies must be dosed four to nine times per day for the treatment of PAH. Reducing dose frequency has the potential to ease patient burden and improve compliance. Additionally, we believe that INS1009 may be associated with fewer side effects, including elevated heart rate, low blood pressure, and severity and/or frequency of cough, associated with high initial drug levels and local upper airway exposure when using current inhaled prostanoid therapies. We believe INS1009 may offer a differentiated product profile for rare pulmonary disorders, including PAH, and we are currently evaluating our options to advance its development, including exploring its use as an inhaled dry powder formulation.

Phase 1 Study Results

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

We have completed a phase 1 study of INS1009. The phase 1 study was a randomized, double-blind, placebo-controlled single ascending dose study of INS1009 for inhalation to determine its safety, tolerability, and pharmacokinetics in healthy volunteers. Twenty-four (24) patients were enrolled and received INS1009 with cohorts of eight patients receiving doses of 85 micrograms (mcg), 170 mcg, 340 mcg or placebo. Participants in the first cohort (8 patients) received a single dose of open label treprostinil (Tyvaso) at 54 mcg 24 hours prior to receiving INS1009 at 85 mcg. The 85 mcg dose of INS1009 provides an equivalent amount of treprostinil on a molar basis as the 54 mcg dose of Tyvaso. The peak serum concentration was approximately 90% lower for treprostinil after INS1009 administration compared with Tyvaso, which could indicate a reduced future adverse event (AE) profile. The pharmacokinetic characteristics also supported once- or twice-daily dosing. The longer half-life of treprostinil for INS1009 was likely due to a sustained pulmonary release. The AE profile was consistent with other inhaled prostanoids. These data were presented at the European Respiratory Society international congress in September 2016.

KEY COMPONENTS OF OUR STATEMENT OF OPERATIONS

Research and Development (R&D) Expenses

R&D expenses consist of salaries, benefits and other related costs, including stock-based compensation, for personnel serving in our research and development functions, including medical affairs. Expenses also include other internal operating expenses, the cost of manufacturing our drug candidate(s) for clinical study, the cost of conducting clinical studies, and the cost of conducting preclinical and research activities. In addition, our R&D expenses include payments to third parties for the license rights to products in development (prior to marketing approval), such as for INS1007. Our expenses related to manufacturing our drug candidate(s) for clinical study are primarily related to activities at CMOs that manufacture our product candidates for our use, including purchases of active pharmaceutical ingredients. Our expenses related to clinical trials are primarily related to activities at contract research organizations that conduct and manage clinical trials on our behalf.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits and other related costs, including stock-based compensation, for our non-employee directors and personnel serving in our executive, finance and accounting, legal, pre-commercial, corporate development, information technology, program management and human resource functions. General and administrative expenses also include professional fees for legal services, including fees incurred in connection with the securities litigation filed against us and patent-related expenses, consulting services including for pre-commercial planning activities such as non-branded disease awareness, insurance, board of director fees, tax and accounting services.

Investment Income and Interest Expense

Investment income consists of interest and dividend income earned on our cash and cash equivalents. Interest expense consists primarily of interest costs and amortization of debt issuance costs related to our debt obligations. Debt issuance costs are amortized to interest expense using the effective interest rate method over the term of the debt. Our balance sheet reflects debt, net of debt issuance costs paid to the lender and other third party costs. Unamortized debt issuance costs associated with extinguished debt are expensed in the period of the extinguishment.

RESULTS OF OPERATIONS

Comparison of the Three Months Ended September 30, 2017 and 2016

Net Loss

Net loss for the quarter ended September 30, 2017 was $45.2 million , or $0.69 per share—basic and diluted, compared with a net loss of $37.8 million , or $0.61 per share—basic and diluted, for the quarter ended September 30, 2016 . The $7.4 million increase in our net loss for the quarter ended September 30, 2017 as compared to the same period in 2016 was primarily due to:

- Increased research and development expenses of $3.2 million , primarily resulting from an increase in expenses related to INS1007 and ALIS clinical trial expenses; and
- Increased general and administrative expenses of $3.7 million , resulting from an increase in consulting fees relating to pre-commercial planning activities and higher compensation and related expenses due to an increase in headcount.

In addition, there was a $0.7 million increase in interest expense resulting from the increase in our debt in the second half of 2016.

Research and Development Expenses

Research and development expenses for the quarters ended September 30, 2017 and 2016 were comprised of the following (in thousands):

	Quarters Ended September 30,		Increase (decrease)	
	2017	2016	$	%
External Expenses				
Clinical development & research	$ 12,307	$ 9,628	$ 2,679	27.8 %
Manufacturing	2,884	2,967	(83)	(2.8)%
Regulatory and quality assurance	1,100	401	699	174.3 %
Subtotal—external expenses	$ 16,291	$ 12,996	$ 3,295	25.4 %
Internal Expenses				
Compensation and related expenses	$ 8,373	$ 8,086	$ 287	3.5 %
Other internal operating expenses	2,011	2,351	(340)	(14.5)%
Subtotal—internal expenses	$ 10,384	$ 10,437	$ (53)	(0.5)%
Total	$ 26,675	$ 23,433	$ 3,242	13.8 %

Research and development expenses increased to $26.7 million during the quarter ended September 30, 2017 from $23.4 million in the same period in 2016 . The $3.2 million increase was primarily due to an increase of $2.7 million in external clinical development expenses, specifically $2.1 million of start-up phase 2 clinical trial expenses related to INS1007 and $2.0 million of ALIS clinical trial expenses, partially offset by a $1.4 million decrease in INS1009 research expenses. In addition, regulatory and quality assurance expenses increased by $0.7 million primarily due to ALIS regulatory consulting and publication expenses in the quarter ended September 30, 2017 as compared to the prior year period.

General and Administrative Expenses

General and administrative expenses for the quarter ended September 30, 2017 and 2016 were comprised of the following (in thousands):

	Quarters Ended September 30,		Increase (decrease)	
	2017	2016	$	%
General & administrative	$ 9,355	$ 9,097	$ 258	2.8%
Pre-commercial expenses	8,053	4,619	3,434	74.3%
Total general & administrative expenses	$ 17,408	$ 13,716	$ 3,692	26.9%

General and administrative expenses increased to $17.4 million during the quarter ended September 30, 2017 from $13.7 million in the same period in 2016 . The $3.7 million increase was primarily due to an increase of $2.3 million in consulting fees relating to pre-commercial planning activities, including non-branded disease awareness and other professional fees, and an increase of $0.9 million due to higher compensation costs related to an increase in headcount.

Interest Expense

Interest expense was $1.5 million for the quarter ended September 30, 2017 as compared to $0.8 million in the same period in 2016 . The $0.7 million increase in interest expense in the quarter ended September 30, 2017 as compared to the prior year quarter relates to an increase in borrowings from Hercules Capital, Inc. (Hercules) during September and October of 2016. We entered into an Amended and Restated Loan Agreement (A&R Loan Agreement) with Hercules in September 2016 which increased our borrowing capacity by an additional $30.0 million to an aggregate total of $55.0 million, and we used this increased borrowing capacity to fund the upfront payment to AstraZeneca for the exclusive global rights to INS1007 in October 2016.

Comparison of the Nine Months Ended September 30, 2017 and 2016

Net Loss

Net loss for the nine months ended September 30, 2017 was $127.3 million , or $2.01 per share—basic and diluted, compared with a net loss of $107.9 million , or $1.74 per share—basic and diluted, for the nine months ended September 30, 2016 . The $19.4 million increase in our net loss for the nine months ended September 30, 2017 as compared to the same period in 2016 was primarily due to:

- Increased R&D expenses of $7.9 million , primarily resulting from an increase in expenses related to INS1007 and higher compensation and related expenses due to an increase in headcount as compared to the prior period, partially offset by decreases in INS1009 research expenses; and

- Increased general and administrative expenses of $9.3 million , primarily resulting from an increase in pre-commercial planning activities and higher compensation and related expenses due to an increase in headcount.

In addition, there was a $2.4 million increase in interest expense resulting from the increase in our debt in the second half of 2016.

Research and Development Expenses

Research and development expenses for the nine months ended September 30, 2017 and 2016 were comprised of the following (in thousands):

	Nine Months Ended September 30,		Increase (decrease)	
	2017	2016	$	%
External Expenses				
Clinical development & research	$ 30,614	$ 26,266	$ 4,348	16.6 %
Manufacturing	10,490	12,243	(1,753)	(14.3)%
Regulatory and quality assurance	2,996	1,366	1,630	119.3 %
Subtotal—external expenses	$ 44,100	$ 39,875	$ 4,225	10.6 %
Internal Expenses				
Compensation and related expenses	$ 24,071	$ 21,463	$ 2,608	12.2 %
Other internal operating expenses	7,629	6,513	1,116	17.1 %
Subtotal—internal expenses	$ 31,700	$ 27,976	$ 3,724	13.3 %
Total	$ 75,800	$ 67,851	$ 7,949	11.7 %

Research and development expenses increased to $75.8 million during the nine months ended September 30, 2017 from $67.9 million in the same period in 2016 . The $7.9 million increase was due to a $4.3 million increase in external clinical development expenses, specifically $5.1 million of start-up phase 2 clinical trial expenses related to INS1007 and $1.9 million of ALIS clinical trial expenses, which were partially offset by a $2.6 million decrease in INS1009 research expenses. In addition, compensation and related expenses increased by $2.6 million due to an increase in headcount. There were also increases in regulatory and quality assurance expenses of $1.6 million , primarily due to increases in ALIS clinical consulting. These increases were partially offset by a $1.8 million decrease in manufacturing expenses due to a $3.0 million reduction in ALIS production-related expenses, which was partially offset by purchases of $1.2 million of clinical materials related to INS1007 in the second quarter of 2017.

General and Administrative Expenses

General and administrative expenses for the nine months ended September 30, 2017 and 2016 were comprised of the following (in thousands):

	Nine Months Ended September 30,		Increase (decrease)	
	2017	2016	$	%
General & administrative	$ 27,364	$ 26,789	$ 575	2.1%
Pre-commercial expenses	20,403	11,709	8,694	74.3%
Total general & administrative expenses	$ 47,767	$ 38,498	$ 9,269	24.1%

General and administrative expenses increased to $47.8 million during the nine months ended September 30, 2017 from $38.5 million in the same period in 2016. The $9.3 million increase was primarily due to an increase of $6.2 million in

consulting fees relating to pre-commercial planning activities, including non-branded disease awareness and other professional fees, and an increase of $2.5 million due to higher compensation expenses related to an increase in headcount.

Interest Expense

Interest expense was $4.5 million during the nine months ended September 30, 2017 as compared to $2.0 million in the same period in 2016. This increase in interest expense relates primarily to the increase in our borrowings from Hercules in September and October of 2016.

LIQUIDITY AND CAPITAL RESOURCES

Overview

There is considerable time and cost associated with developing a potential drug or pharmaceutical product to the point of regulatory approval and commercialization. We had $ 430.7 million in cash and cash equivalents as of September 30, 2017 and reported a net loss of $127.3 million for the nine months ended September 30, 2017 . Historically we have funded our operations through public offerings of equity securities and debt financings. To date, we have not generated material revenue from ALIS. We do not expect to generate revenue unless or until marketing approval is received for ALIS. Accordingly, we expect to continue to incur losses while funding R&D activities, regulatory submissions, potential commercial launch activities and general and administrative expenses. We expect our future cash requirements to be substantial, and we will need to raise additional capital to fund operations, to develop and commercialize ALIS, to develop INS1007 and INS1009 and to develop, acquire, in-license or co-promote other products that address orphan or rare diseases.

We believe we currently have sufficient funds to meet our financial needs for at least the next 12 months. In September 2017, we completed an underwritten offering of 14.1 million shares of our common stock for net proceeds of $377.7 million, net of fees and expenses related to the offering. We will be opportunistic in raising additional capital within the next 12 months and may do so through equity or debt financing(s), strategic transactions or otherwise. The source, timing and availability of any future financing or other transaction will depend principally upon continued progress in our regulatory, development and pre-commercial activities. Any equity or debt financing(s) will also be contingent upon equity and debt market conditions and interest rates at the time. We cannot assure you that adequate capital will be available on favorable terms, or at all, when needed. If we are unable to obtain sufficient additional funds when required, we may be forced to delay, restrict or eliminate all or a portion of our R&D programs, pre-commercialization activities, or dispose of assets or technology. The source, timing and availability of any future financing or other transaction will depend on and will likely be affected by a number of factors, including:

- the timing and cost of our current and anticipated clinical trials of ALIS for the treatment of patients with NTM lung infections;
- the decisions of the FDA, MHLW and EMA with respect to our potential applications for marketing approval of ALIS in the US, Japan and Europe, respectively; the costs of activities related to the regulatory approval process; and the timing of approvals, if received;
- the costs associated with commercializing ALIS, if we receive marketing approvals; including the costs of establishing the sales and marketing capabilities to be prepared for potential commercial launches of ALIS, if approved;
- the cost of filing, prosecuting, defending, and enforcing patent claims;
- the timing and cost of our anticipated clinical trials, including for INS1007 and the related milestone payments due to AstraZeneca;
- the costs of our manufacturing-related activities, including an increase in commercial inventory production and expansion projects related to our production capabilities; and
- subject to receipt of marketing approval, the levels, timing and collection of revenue received from sales of approved products, if any, in the future.

Cash Flows

As of September 30, 2017 , we had cash and cash equivalents of $ 430.7 million , as compared with $ 162.6 million as of December 31, 2016 . The $ 268.1 million increase was due primarily to the cash proceeds from our issuance of common stock in September 2017, partially offset by use of cash in operating activities. Our working capital was $ 408.7 million as of September 30, 2017 as compared with $ 140.4 million as of December 31, 2016 .

Net cash used in operating activities was $ 111.4 million and $ 88.7 million for the nine months ended September 30, 2017 and 2016 , respectively. The net cash used in operating activities during the nine months ended September 30, 2017 and 2016 was primarily for the clinical, manufacturing and pre-commercial activities related to ALIS, as well as general and administrative expenses. In addition, net cash used in operating activities during the nine months ended September 30, 2017 included start-up clinical trial expenses related to INS1007.

Net cash used in investing activities was $ 1.3 million and $ 3.4 million for the nine months ended September 30, 2017 and 2016 , respectively. The net cash used in investing activities was primarily related to payments for the build out of our headquarters and lab facilities in Bridgewater, New Jersey.

Net cash provided by financing activities was $ 380.7 million and $ 9.8 million for the nine months ended September 30, 2017 and 2016 , respectively. Net cash provided by financing activities for the nine months ended September 30, 2017 included net cash proceeds of $377.7 million from our issuance of 14.1 million shares of common stock in September 2017 and cash proceeds received from stock option exercises. Net cash provided by financing activities for the nine months ended September 30, 2016 was primarily net cash proceeds from the issuance of debt.

We expect our operating expenses and capital expenditures will significantly increase in 2018 as compared to 2017 as a result of our investments in preparation for commercialization of ALIS in the US, ongoing and future clinical trials and general and administrative activities.

Contractual Obligations

There were no material changes outside of the ordinary course of business in our contractual obligations during the nine months ended September 30, 2017 from those disclosed in Item 7, “Management’s Discussion and Analysis of Financial Condition and Results of Operations-Liquidity and Capital Resources - Contractual Obligations” in our Annual Report on Form 10-K for the year ended December 31, 2016, except for the following:

In September 2017, we increased our purchase commitments made in the normal course of business with CMOs and various other suppliers related to the production requirements for ALIS. These purchase commitments have increased as a result of the release of top-line results from the CONVERT study.

As of September 30, 2017 , future payments under our long-term debt agreements, capital leases, minimum future payments under non-cancellable operating leases and minimum future payment obligations are as follows:

	Total	Less than 1 year	1 - 3 Years	4 - 5 Years	After 5 Years
			(in thousands)		
Debt obligations					
Debt maturities	$ 55,000	$ —	$ 29,504	$ 25,496	$ —
Contractual interest	16,157	5,158	8,520	2,479	—
Operating leases	4,293	1,511	2,162	620	—
Purchase obligations	6,075	2,700	3,375	—	—
Total contractual obligations	$ 81,525	$ 9,369	$ 43,561	$ 28,595	$ —

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

In October 2017, we exercised an option to buy-down the future royalties that will be payable to PARI. Pursuant to the existing licensing agreement, PARI is entitled to receive royalty payments in the mid-single digits on the annual global net sales

of ALIS, subject to certain specified annual minimum royalties. The royalty buy-down will enable us to reduce the royalty payments due to PARI based on the annual global net sales of ALIS. The payment to PARI will be included as a component of general and administrative expenses in the fourth quarter of 2017.

In October 2017, we entered into certain agreements with Patheon UK Limited (Patheon) related to increasing our long-term production capacity for ALIS commercial inventory. The agreements provide for Patheon to manufacture and supply ALIS for our anticipated commercial needs. Under these agreements, we are required to deliver to Patheon the required raw materials, including active pharmaceutical ingredients, and certain fixed assets needed to manufacture ALIS. Patheon's supply obligation will commence once certain technology transfer and construction services are completed. Our manufacturing and supply agreement with Patheon will remain in effect for a fixed initial term, after which it will continue for successive renewal terms unless either we or Patheon have given written notice of termination. The technology transfer agreement will expire when the parties agree that the technology transfer services have been completed. The agreements may also be terminated under certain other circumstances, including by either party due to a material uncured breach of the other party or the other party's insolvency. These early termination clauses may reduce the amounts due to the relevant parties. The investment in our long-term production capacity build-out, including under the Patheon agreements and related agreements or purchase orders with third parties for raw materials and fixed assets will be incurred over the next three to four years.

Off-Balance Sheet Arrangements

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

CRITICAL ACCOUNTING POLICIES

There have been no material changes to our critical accounting policies as disclosed in our Annual Report on Form 10-K for the year ended December 31, 2016 . For the required interim updates of our accounting policies, see Note 2 to our Consolidated Financial Statements — "Summary of Significant Accounting Policies" in this Quarterly Report on Form 10-Q.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As of September 30, 2017 , our cash and cash equivalents were in cash accounts or were invested in money market funds. Such accounts or investments are not insured by the federal government.

As of September 30, 2017 , we had $ 55.0 million of borrowings outstanding that currently bear interest at 9.25% under the A&R Loan Agreement with Hercules. If a 10% change in interest rates had occurred on September 30, 2017 , this change would not have had a material effect on the fair value of our debt as of that date, nor would it have had a material effect on our future earnings or cash flows.

The majority of our business is conducted in US dollars. However, we do conduct certain transactions in other currencies, including Euros, British Pounds, and Japanese Yen. Historically, fluctuations in foreign currency exchange rates have not materially affected our results of operations and during the three and nine months ended September 30, 2017 and 2016 , our results of operations were not materially affected by fluctuations in foreign currency exchange rates.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

Our management, under the supervision and with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2017 . The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities and Exchange Act of 1934, as amended (the Exchange Act), means controls and other procedures that are designed to provide reasonable assurance that information required to be disclosed by us in the periodic reports that we file or submit with the SEC is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and to ensure that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure. Based on that evaluation as of September 30, 2017 , our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures are effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) under the Exchange Act) during the three months ended September 30, 2017 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

See Note 9 to our Consolidated Financial Statements — "Commitments and Contingencies — Legal Proceedings" in this Quarterly Report on Form 10-Q for a description of our material legal proceedings. From time to time, we are also party to various lawsuits, claims and other legal proceedings that arise in the ordinary course of our business. While the outcomes of these matters are uncertain, management does not expect that the ultimate costs to resolve these matters will have a material adverse effect on our consolidated financial position, results of operations or cash flows.

ITEM 1A. RISK FACTORS

Our business is subject to substantial risks and uncertainties. You should carefully consider the risk factors set forth below as well as the other information contained in this Quarterly Report on Form 10-Q and in our other public filings in evaluating our business, including our Annual Report on Form 10-K for the year ended December 31, 2016, which was filed with the SEC on February 23, 2017. Any of the risks and uncertainties described below, either alone or taken together, could materially and adversely affect our business, financial condition, results of operations, prospects for growth, and the value of an investment in our common stock. In addition, these risks and uncertainties could cause actual results to differ materially from those expressed or implied by forward-looking statements contained in this Quarterly Report on Form 10-Q (please read the Cautionary Note Regarding Forward-Looking Statements). The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operation, prospects and the value of an investment in our common stock and could cause actual results, performance or achievements to differ materially from those expressed or implied by forward-looking statements.

Risks Related to Development, 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 an 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 concluded that the data submitted did not provide enough evidence to support an approval. We currently expect to submit an NDA to the FDA pursuant to Subpart H for ALIS based on the efficacy data from the CONVERT study through month six. Although we view the top-line six-month results from the CONVERT study as promising, the FDA may not agree that these data are 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 are 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 US, 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 US, 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 are 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 US 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 US, 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 US 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) and other applicable standards and regulations.

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 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 US, 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;
- Conditions imposed on us by the FDA or any non-US regulatory authority regarding the scope or design of our clinical trials may require us to collect and submit information to regulatory authorities, ethics committees, 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 Inc., 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, PMDA, 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 US 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 US, Japan, Canada and Australia. The eFlow Nebulizer System is not approved for commercial use in the US, Japan, Canada or certain other markets in which we may seek to commercialize ALIS.

In the US, 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 and collaboration 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. Failure of PARI to successfully supply, or to maintain regulatory approval or clearance, of the eFlow Nebulizer System could result in increased development costs, delays in or failure to obtain regulatory approval, and associated delays in ALIS reaching the market. 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 US 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, 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. For additional information related to long-term commercial production, see *"Management's Discussion and Analysis of Financial Condition and Results of Operations-Contractual Obligations."*

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 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 nine months ended September 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 September 30, 2017, our accumulated deficit was $892.5 million . For the nine months ended September 30, 2017, our consolidated net loss was $127.3 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 September 30, 2017, we had $ 430.7 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 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 $ 55.4 million as of September 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 May 1, 2019. 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 11% of our total assets as of September 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 Inc. 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 US 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 US 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 US 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-US regulatory authorities. In addition, there is a risk that full reimbursement may not be available for high priced products. Moreover, eligibility for coverage does not imply that any product will be reimbursed in all cases or at a rate that allows us to make a profit or even cover our costs. Interim payments for new products, if applicable, also may not be sufficient to cover our costs and may not be made permanent. Subsequent approvals of competitive products could result in a detrimental change to the reimbursement of our products.

There is a significant focus in the US healthcare industry and elsewhere on cost containment and value. We expect changes in the Medicare program and state Medicaid programs, as well as managed care organizations and other third-party payers, to continue to put pressure on pharmaceutical product pricing. 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 US 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 US, including Japan, Canada and the countries in the EU, pricing of pharmaceutical products is subject to governmental control. Evaluation criteria used by many EU government agencies for the purposes of pricing and reimbursement typically focus on a product's degree of innovation and its ability to meet a clinical need unfulfilled by currently available therapies. The 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 US physicians and teaching hospitals as well as investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties. The reported data are 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 US 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 US for our proposed trade names. Any failure or delay associated with such approvals may delay the commercialization of our products.

Any trade name we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the US Patent and Trademark Office (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 US, we are subject to various federal and state health care "fraud and abuse" laws, including anti-kickback laws, false claims laws and other laws intended to reduce fraud and abuse in federal and state health care programs. 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 US 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 US 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. US patents and patent applications may also be subject to interference or derivation proceedings, and US patents may be subject to re-examination proceedings, reissue, post-grant review and/or *inter partes* review in the 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 US 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 US 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 US 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 treprostinil. Our supply of the active pharmaceutical ingredient for INS1009 is dependent upon a single supplier. The supplier owns patents on its manufacturing process, and we have filed patent applications for INS1009; 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 and see Note 10, Subsequent Event, in Item 1 Part I of this Quarterly Report on Form 10Q. 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 US 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 US 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 US 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, and that we, certain of our executive officers and the underwriters violated Section 10(b) of 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 this Quarterly Report on Form 10-Q. 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 US. As of September 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 US 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 US;

- 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 US 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 US 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 US 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 US 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 US Department of Commerce’s Bureau of Industry and Security, the US Department of Treasury’s Office of Foreign Assets Control, and various non-US 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 US 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.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

There were no unregistered sales of the Company’s equity securities during the quarter ended September 30, 2017 .

ITEM 6. EXHIBITS

Exhibit Index

3.1	Articles of Incorporation of Insmed Incorporated, as amended through June 14, 2012 (incorporated by reference from Exhibit 3.1 to Insmed Incorporated's Annual Report on Form 10-K filed on March 18, 2013).
3.2	Amended and Restated Bylaws of Insmed Incorporated (incorporated by reference from Exhibit 3.1 to Insmed Incorporated's Quarterly Report on Form 10-Q filed on August 6, 2015).
10.1*	Amendment No. 7 to License Agreement between Transave, Inc. and PARI Pharma GmbH, effective as of July 21, 2017.
10.2*	Amendment No. 1 to Commercialization Agreement between Insmed Incorporated and PARI Pharma GmbH, effective as of July 21, 2017.
31.1	Certification of William H. Lewis, Chief Executive Officer of Insmed Incorporated, pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes Oxley Act of 2002.
31.2	Certification of Paolo Tombesi, Chief Financial Officer (Principal Financial and Accounting Officer) of Insmed Incorporated, pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes Oxley Act of 2002.
32.1	Certification of William H. Lewis, Chief Executive Officer of Insmed Incorporated, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2002.
32.2	Certification of Paolo Tombesi (Principal Financial and Accounting Officer) of Insmed Incorporated, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2002.
101	The following materials from Insmed Incorporated's quarterly report on Form 10-Q for the quarter ended September 30, 2017 formatted in XBRL (eXtensible Business Reporting Language): (i) Consolidated Balance Sheets as of September 30, 2017 and December 31, 2016, (ii) Consolidated Statements of Comprehensive Loss for the three and nine months ended September 30, 2017 and 2016, (iii) Consolidated Statements of Cash Flows for the nine months ended September 30, 2017 and 2016, and (iv) Notes to the Unaudited Consolidated Financial Statements.
*	Confidential treatment has been requested for certain portions of this exhibit. The confidential portions of this exhibit have been omitted and filed separately with the Securities and Exchange Commission.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

INSMED INCORPORATED

Date: November 2, 2017

By /s/ Paolo Tombesi

Paolo Tombesi
Chief Financial Officer
(Principal Financial and Accounting Officer)

CONFIDENTIAL TREATMENT HAS BEEN REQUESTED AS TO CERTAIN PORTIONS OF THIS DOCUMENT. EACH SUCH PORTION, WHICH HAS BEEN OMITTED HEREIN AND REPLACED WITH ASTERISKS (***), HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

AMENDMENT NO. 7
TO LICENSE AGREEMENT BETWEEN
INSMED INCORPORATED AND PARI PHARMA GMBH

This seventh amendment (" **Amendment No. 7** ") effective 21 July 2017 (" **Amendment No. 7 Effective Date** ") to the License Agreement dated and effective the 25 th of April 2008 between PARI Pharma GmbH, a German corporation with a principal place of business at Moosstrasse 3, D-82319 Starnberg, Germany (" **PARI** ") and Transave, Inc., a Delaware corporation, as amended by Amendment No. 1 the 24 th day of June 2009, Assignment and Amendment No. 2 the 22 nd day of December 2010, Amendment No. 3 the 6 th day of March 2012, Amendment No. 4 the 21 st day of May 2012, Amendment No. 5 the 5 th day of October 2015 and Amendment No. 6 the 9 th day of October 2015 (collectively, the " **Agreement** "), is entered into between PARI and Insmed Incorporated (successor in interest to Transave, Inc.), with registered offices at 10 Finderne Avenue, Building 10, Bridgewater, NJ 08807-3365 (" **Insmed** "). PARI and Insmed shall be referred to collectively as the " **Parties** ".

WHEREAS, the Parties now desire to amend the terms and conditions of the Agreement to reflect certain business discussions between the Parties and the current development status of the Drug Product.

NOW, THEREFORE, in consideration of the recitals set forth above, the mutual covenants, terms and conditions set forth below, and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties agree as follows:

1. Definitions. Capitalized terms used but not defined in this Amendment No. 7 shall have the meanings ascribed to them in the Agreement.

2. Section 2.6. Section 2.6 of the Agreement is hereby amended by deleting "[***]" and replacing it with "as set forth in Section 6.1 below".

3. Section 6.1. Section 6.1 of the Agreement is hereby deleted in its entirety and replaced with the following:

6.1 **Royalties for Drug Products.**

(a) In further consideration of the rights and license granted by PARI under this Agreement, during the Royalty Term, subject to the terms and conditions of this Agreement, Insmed agrees to pay PARI a royalty equal to [***] of the Net Sales of Drug

*** Certain information on this page has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

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

(b) Within thirty (30) days of releasing top line results (which indicate whether the primary endpoint was met) via a press release for INS-212, the Phase III clinical trial entitled *Study to Evaluate Efficacy of LAI When Added to Multi-drug Regimen Compared to Multi-drug Regimen Alone (CONVERT)* but in no event later than March 31, 2018 (the "Royalty Buy-Down Exercise Period"), Insmed, in exchange for a [***] payment to PARI (the " **Option Payment** "), shall have the option, in its sole discretion, to replace the [***] with the following [***] (the "Royalty Buy-Down Option"):

[***]	[***]
[***]	[***]
[***]	[***]

(c) Insmed shall exercise the Royalty Buy-Down Option by notifying PARI in writing within the Royalty Buy-Down Exercise Period and, if Insmed exercises the option, the Option Payment shall be due and payable within [***] business days from the exercise of the Royalty Buy-Down Option. For clarity, the Option Payment shall only be payable if Insmed, in its sole discretion, elects to exercise the option set forth above.

4. Section 7.2A(a). Section 7.2A(a) of the Agreement is hereby amended by deleting it in its entirety and replacing it with the following:

(a) The Parties agree that Insmed will use Commercially Reasonable Efforts to meet the following milestones with respect to NTM:

Milestone Activity	**Milestone Deadline**
Completion of the INS-212 Clinical Study Report (CSR)	[***]
Completion of submission to US FDA for the Drug Product in NTM	[***]
First Commercial Sale of the Drug Product in US in NTM	[***]
Approval of an MAA by the European Medicines Agency for the Drug Product	[***]

If Insmed fails to meet a milestone within the applicable time period, other than any failure resulting from a breach of this Agreement by PARI, then, subject to the provisions of Section 7.3, PARI shall have the option to render Insmed's license hereunder non-exclusive solely with respect to NTM and to terminate its obligation not to compete with Insmed in NTM as set forth in Section 4.2 of this Agreement. Such option must be exercised by sending the Diligence Termination Notice to Insmed, and shall become effective on the [***] day following the date of the Diligence Termination Notice. If such

milestone is still not met within [***] months of the applicable time period, other than any failure resulting from a breach of this Agreement by PARI, then, subject to the provisions of Section 7.3, PARI shall have the option to terminate the license granted to Insmed under this Agreement with respect to NTM only by providing written notice thereof to Insmed.

PARI's options to render the license granted hereunder non-exclusive, to terminate its obligations to not compete with Insmed or to terminate the license as described in this Section shall only apply to (i) the US in case Insmed fails to meet the milestones for the US, (ii) Europe in case Insmed fails to meet the milestone for the EU; or (iii) the Territory in case both (i) and (ii) above occur.

If the diligence milestone First Commercial Sale of the Drug Product in the US in NTM is not met [***] months after the applicable milestone deadline as set forth in the table above and First Commercial Sale of the Drug Product in the US did not occur or commercial sale has been ceased for another indication in the US, PARI shall be free to terminate the entire License with respect to US.

If the diligence milestone First Commercial Sale of the Drug Product in the EU in NTM is not met [***] months after the applicable milestone deadline as set forth in the table above and First Commercial Sale of the Drug Product did not occur or commercial sale has been ceased for another indication in the EU, PARI shall be free to terminate the entire License with respect to Europe.

In case the preconditions for the termination of the entire license in all regions, the US and Europe as set forth above, are given, PARI shall be free to terminate the entire license with respect to the Territory."

5. Section 5.2. The table in Section 5.2 of the Agreement is hereby deleted it in its entirety and replaced with the following (milestone events and payments one and two have been fulfilled and therefore shown as strikethrough):

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

6. Section 7.2 . The table in Section 7.2(a) is hereby deleted it in its entirety and replaced with the following:

Milestone Activity	Milestone Deadline
a. **Diligence Milestone 1** : initiation of First Phase III Trial for Bronchiectasis	[***]

Within [***] days following the final results of the Phase III Trial for Bronchiectasis, the Parties, acting in good faith, will negotiate reasonable additional milestones.

7. Section 7.2C. The Agreement is hereby amended by adding a new Section 7.2C:

7.2C **Diligence Obligations.** If Insmed fails to achieve one of the diligence obligations for NTM and one of the diligence obligations for Bronchiectasis as set forth in the tables in Sections 7.2(a) and 7.2A(a), and if such milestones are still not met within [***] months of the applicable time period, other than due to any failure resulting from a breach of this Agreement by PARI, then, subject to the provisions of Section 7.3, PARI shall have the option to terminate this Agreement in its entirety by providing written notice thereof to Insmed, regardless whether or not PARI previously exercised any of its rights to render the license granted to Insmed under this Agreement non-exclusive or to terminate such license, both of the foregoing, with respect to a certain indication.

8. Section 15.4 . A new introduction to the first sentence of Section 15.4 shall be added as follows:

"In addition to PARI's right to terminate this Agreement as set forth elsewhere in this Agreement,"

Section 15.4(ii) of the Agreement shall hereby be amended by deleting "[***]" and replacing it with "[***]".

9. Miscellaneous. Upon execution, this Amendment No. 7 shall be made part of the Agreement and shall be incorporated therein by reference. Except as provided herein, all other terms and conditions of the Agreement shall remain in full force and effect.

IN WITNESS WHEREOF, the Parties have executed this Amendment No. 7 as of the Amendment No. 7 Effective Date indicated above.

INSMED INCORPORATED **PARI PHARMA GMBH**

By: _____ By: _____

Name: William H. Lewis Name: Dr. Martin Knoch

Title: CEO & President Title: President

Date: _____ Date: _____

*** Certain information on this page has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

CONFIDENTIAL TREATMENT HAS BEEN REQUESTED AS TO CERTAIN PORTIONS OF THIS DOCUMENT. EACH SUCH PORTION, WHICH HAS BEEN OMITTED HEREIN AND REPLACED WITH ASTERISKS (***), HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.

AMENDMENT NO. 1
TO COMMERCIALIZATION AGREEMENT BETWEEN INSMED INCORPORATED AND PARI PHARMA GMBH

This first amendment (" **Amendment No. 1** ") effective 21 July 2017 (" **Amendment No. 1 Effective Date** ") to the Commercialization Agreement dated and effective the 8 th of July 2014 (the " **Agreement** ") between PARI Pharma GmbH, a German corporation with a principal place of business at Moosstrasse 3, D-82319 Starnberg, Germany (" **PARI** ") and Insmed Incorporated, a Virginia corporation with a principal place of business at 10 Finderne Avenue, Building 10, Bridgewater, NJ 08807-3365 (" **Insmed** "), is entered into between PARI and Insmed. PARI and Insmed shall be referred to collectively as the " **Parties** ".

WHEREAS, the Parties now desire to amend the terms and conditions of the Agreement to reflect certain business discussions between the Parties.

NOW, THEREFORE, in consideration of the recitals set forth above, the mutual covenants, terms and conditions set forth below, and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Parties agree as follows:

1. Definitions. Capitalized terms used but not defined in this Amendment No. 1 shall have the meanings ascribed to them in the Agreement.

2. Section 1.14 shall be deleted and replaced as follows:

" **1.14 "** [***] **"** shall mean a unit of Device which comprises of [***]."

3. Section 4.3. Section 4.3(c) of the Agreement is hereby amended by adding the following at the end of such subsection: "If there are material changes in the applicable tax laws during the Term, the parties shall negotiate in good faith to determine whether any amendments are required to the terms of this Agreement".

4. Section 6.1. Section 6.1 of the Agreement is hereby amended by deleting "Within [***] days from the Effective Date" and replacing it with "Prior to the first MAA submission".

5. Section 6.2. Section 6.2 of the Agreement is hereby deleted in its entirety and replaced with the following:

"6.2 Forecasts . Subject to Section 6.3 with respect to the Initial Purchase Order, no less than [***] months (for the United States) or [***] months (for any major market such as the EU or Japan other than the United States) prior to the earliest anticipated delivery date of the Initial Purchase Order and thereafter on a quarterly basis during the Term, at least [***] days

before the end of each calendar quarter, INSMED shall provide PARI with its good faith, reasonable written projections (broken down by Devices, [***] and [***]) of the anticipated total market requirements of PARI Products for each major market (such as the United States, the EU or Japan) in the INSMED Territory (" **Forecast** "), on a [***] basis during the [***] month period immediately following (i) the calendar quarter in which such projection is issued or (ii) in case of the first Forecast for the First Commercial Sale in each major market (such as the EU or Japan). The forecasted quantities of PARI Products set forth in each Forecast for (i) the first [***] month period in such Forecast are binding and (ii) [***] in such Forecast are non-binding, good faith estimates provided solely to assist PARI in its production planning. All Forecasts shall be deemed INSMED Confidential Information. PARI shall use commercially reasonable efforts to commence scale-up activities to transition from clinical supply to commercial supply based on INSMED's Forecasts which shall be reasonably explained by INSMED to PARI."

6. Section 6.3 . The first sentence of Section 6.3 is hereby deleted and replaced as follows:

"No later than [***] months (for the United States) or [***] months (for each major market such as the EU or Japan other than the United States) prior to the earliest anticipated delivery date of the Initial Purchase Order, INSMED shall provide PARI with a purchase order for a quantity by item number of PARI Products needed for initial supply of INSMED Product and PARI Products in the respective major market (such as the United States, the EU or Japan) (each an " **Initial Purchase Order** "). For the Initial Purchase Order for the United States, PARI shall deliver (i) at least [***] of the quantity ordered in the Initial Purchase Order within [***] months of the Initial Purchase Order, (ii) at least [***] of the quantity ordered in the Initial Purchase Order within [***] months, of the Initial Purchase Order and (iii) the remaining [***] shall be delivered within [***] months of the Initial Purchase Order. The Parties agree that the above-mentioned lead times for the Initial Purchase Order are based on an assumed demand of aerosol heads in the Initial Purchase Order for the United States which does not exceed [***] aerosol heads in aggregate. In case the actual amount of aerosol heads in the Initial Purchase Order for the United States exceeds [***] aerosol heads in aggregate the Parties will discuss in good faith an adapted delivery."

7. Section 6.4. Section 6.4 (a) is hereby amended by deleting in the third sentence "that no such Purchase Order shall have a shipment date prior to the [***] day following the date of receipt by PARI of the Initial Purchase Order" and replacing it by "that no such Purchase Order shall have a shipment date prior to the earliest anticipated delivery date of the Initial Purchase Order and further provided that the quantities of PARI Products stipulated in an Purchase Order for delivery in the first [***] months after the First Commercial Sale in a major market (such as the EU or Japan) do not exceed the quantities of PARI Products stipulated in the first Forecast which is provided to PARI at least [***] months for the United States and [***] months for other major markets (such as the EU or Japan) prior to the earliest anticipated delivery date of the Initial Purchase Order" so that such third sentence of Section 6.4 (a) reads:

"PARI shall ship the quantity of PARI Products specified in each Purchase Order no less than [***] days after the date and confirmation of such Purchase Order by PARI, unless otherwise agreed to by PARI and INSMED; provided, however, that no such Purchase Order shall have a shipment date prior to the earliest anticipated delivery date of the Initial Purchase Order and further provided that the quantities of PARI Products stipulated in a Purchase Order for delivery in the first [***] months after the First Commercial Sale in a major market (such as the EU or Japan) do not exceed the quantities of PARI Products stipulated in the first Forecast which is provided to PARI at least [***] months for the United States and [***] months for other major markets (such as the EU or Japan) prior to the earliest anticipated delivery date of the Initial Purchase Order."

8. Exhibit D. Exhibit D to the Agreement is hereby amended by deleting it in its entirety and replacing it with Exhibit D attached hereto.

9. Exhibit E. Exhibit E to the Agreement is hereby amended by deleting "[***]" and replacing it with "[***]".

10. Exhibit I. Exhibit I to the Agreement is hereby amended by deleting it in its entirety and replacing it with Exhibit I attached hereto.

11. Miscellaneous. Upon execution, this Amendment No. 1 shall be made part of the Agreement and shall be incorporated therein by reference. Except as provided herein, all other terms and conditions of the Agreement shall remain in full force and effect.

IN WITNESS WHEREOF, the Parties have executed this Amendment No. 1 as of the Amendment No. 1 Effective Date indicated above.

INSMED INCORPORATED	**PARI PHARMA GMBH**
By: _____	By: _____
Name: William H. Lewis	Name: Dr. Martin Knoch
Title: CEO & President	Title: President
Date: _____	Date: _____

*** Certain information on this page has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

EXHIBIT D

Representatives of the JSC

Joint Steering Committee

PARI: [***], [***] and [***]

INSMED: [***], [***] and [***]

*** Certain information on this page has been omitted and filed separately with the Securities and Exchange Commission. Confidential treatment has been requested with respect to the omitted portions.

EXHIBIT I

Price

1. United States/Canada Price

Description	Prices for United States and Canada
for each unit of [***]*	See table below
for each unit of [***]	$[***]

The price for each [***] shall be determined as follows:

Number of [***] Purchased in a Calendar Year	Price/ [***]*
[***]-[***]	$[***]
[***]-[***]	$[***]
[***] and over	$[***]

* [***].

2. EU/ROW Price. Prices for EU and ROW markets shall be negotiated in good faith and set forth in the applicable Territory-Specific Appendix.

EXHIBIT 31.1

Section 302 Certification

I, William H. Lewis, Chief Executive Officer of Insmed Incorporated, certify that:

(1) I have reviewed this Quarterly Report on Form 10-Q of Insmed Incorporated;

(2) Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

(3) Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

(4) The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

(5) The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 2, 2017

/s/ William H. Lewis

William H. Lewis
Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

Section 302 Certification

I, Paolo Tombesi, Chief Financial Officer (Principal Financial and Accounting Officer) of Insmed Incorporated, certify that:

(1) I have reviewed this Quarterly Report on Form 10-Q of Insmed Incorporated;

(2) Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

(3) Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

(4) The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

(5) The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 2, 2017

/s/ Paolo Tombesi

Paolo Tombesi

Chief Financial Officer

(Principal Financial and Accounting Officer)

EXHIBIT 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2003

Solely for the purposes of complying with 18 U.S.C. § 1350, I, William Lewis, Chief Executive Officer of Insmed Incorporated (the "Company"), hereby certify, based on my knowledge, that:

(1) the Quarterly Report on Form 10-Q of the Company for the quarter ended September 30, 2017 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ William H. Lewis

William H. Lewis
Chief Executive Officer
(Principal Executive Officer)

November 2, 2017

This certification accompanies the Quarterly Report on Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Insmed Incorporated under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing. A signed original of this statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

EXHIBIT 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2003

Solely for the purposes of complying with 18 U.S.C. § 1350, I, Paolo Tombesi, Chief Financial Officer (Principal Financial and Accounting Officer) of Insmed Incorporated (the "Company"), hereby certify, based on my knowledge, that:

(1) the Quarterly Report on Form 10-Q of the Company for the quarter ended September 30, 2017 (the "Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Paolo Tombesi

Paolo Tombesi
Chief Financial Officer
(Principal Financial and Accounting Officer)

November 2, 2017

This certification accompanies the Quarterly Report on Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Insmed Incorporated under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing. A signed original of this statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.