INSMED Inc
Form 10-Q
May 07, 2015
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2015

OR

o 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)

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 x No o

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 x No o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a small reporting Company (See the definitions of large accelerated filer, accelerated filer, and small reporting Company in Rule 12b-2 of the Exchange Act).

Large accelerated filer x	Accelerated filer o
Non-accelerated filer o	Small Reporting Company o

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

As of April 30, 2015, there were 61,501,770 shares of the registrant s common stock, $0.01 par value, outstanding.

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INSMED INCORPORATED

FORM 10-Q

FOR THE QUARTER ENDED MARCH 31, 2015

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In this Form 10-Q, we use the words Insmed Incorporated to refer to Insmed Incorporated, a Virginia corporation, and we use the words Company, Insmed, Insmed Incorporated, we, us and our to refer to Insmed Incorporated and its consolidated subsidiaries. IPLEX is a reg trademark of Insmed Incorporated and ARIKAYCE and INSMED 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.

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PART I. FINANCIAL INFORMATION

ITEM 1. CONSOLIDATED FINANCIAL STATEMENTS

INSMED INCORPORATED

Consolidated Balance Sheets

(in thousands, except par value and share data)

	As of March 31, 2015 (unaudited)	As of December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$ 134,554	$ 159,226
Prepaid expenses and other current assets	5,689	5,488
Total current assets	140,243	164,714
In-process research and development	58,200	58,200
Fixed assets, net	7,292	7,534
Other assets	417	416
Total assets	$ 206,152	$ 230,864
Liabilities and shareholders equity		
Current liabilities:		
Accounts payable	$ 7,860	$ 9,249
Accrued expenses	5,976	5,321
Accrued compensation	1,584	4,317
Other current liabilities	716	743
Current portion of long term debt	24,989	
Total current liabilities	41,125	19,630
Other long-term liabilities	162	141
Debt, long-term		24,856
Total liabilities	41,287	44,627
Shareholders equity:		
Common stock, $0.01 par value; 500,000,000 authorized shares, 50,001,770 and 49,806,131 issued and outstanding shares at March 31, 2015 and December 31, 2014, respectively	500	498
Additional paid-in capital	662,514	656,519
Accumulated deficit	(498,149)	(470,780)
Total shareholders equity	164,865	186,237
Total liabilities and shareholders equity	$ 206,152	$ 230,864

See accompanying notes to consolidated financial statements

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INSMED INCORPORATED

Consolidated Statements of Comprehensive Loss (Unaudited)

(in thousands, except per share data)

	Three Months ended March 31,	
	2015	**2014**
Revenues	$	$
Operating expenses:		
Research and development	17,164	11,351
General and administrative	9,542	6,728
Total operating expenses	26,706	18,079
Operating loss	(26,706)	(18,079)
Investment income	23	17
Interest expense	(722)	(606)
Other income (expense), net	36	(19)
Loss before income taxes	(27,369)	(18,687)
Benefit from income taxes		(4,389)
Net loss and comprehensive loss	$ (27,369)	$ (14,298)
Basic and diluted net loss per share	$ (0.55)	$ (0.36)
Weighted average basic and diluted common shares outstanding	49,957	39,240

See accompanying notes to consolidated financial statements

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INSMED INCORPORATED

Consolidated Statements of Cash Flows (Unaudited)

(in thousands)

	Three months ended March 31,	
	2015	**2014**
Operating activities		
Net loss	$ (27,369)	$ (14,298)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	432	167
Stock based compensation expense	4,522	2,358
Amortization of debt discount and debt issuance costs	106	102
Accrual of the end of term charge on the debt	27	33
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(202)	(2,600)
Accounts payable	(1,389)	3,889
Accrued expenses and other current liabilities	1,723	(832)
Accrued compensation	(2,733)	(1,468)
Net cash used in operating activities	(24,883)	(12,649)
Investing activities		
Purchase of fixed assets	(1,264)	(331)
Net cash used in investing activities	(1,264)	(331)
Financing activities		
Payments on capital lease obligations		(16)
Proceeds from exercise of stock options	1,475	353
Net cash provided by financing activities	1,475	337
Decrease in cash and cash equivalents	(24,672)	(12,643)
Cash and cash equivalents at beginning of period	159,226	113,894
Cash and cash equivalents at end of period	$ 134,554	$ 101,251
Supplemental disclosures of cash flow information:		
Cash paid for interest	$ 663	$ 463
Cash received for taxes	$ 994	$ 4,389

See accompanying notes to consolidated financial statements

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INSMED INCORPORATED

NOTES TO UNAUDITED CONSOLIDATED FINANCIAL STATEMENTS

1. The Company and Basis of Presentation

Insmed is a biopharmaceutical company dedicated to improving the lives of patients battling serious and rare lung diseases. The Company is focused on the development and commercialization of ARIKAYCE, or liposomal amikacin for inhalation (LAI), for at least two identified orphan patient populations: patients with nontuberculous mycobacteria (NTM) lung infections and cystic fibrosis (CF) patients with *Pseudomonas aeruginosa (Pseudomonas)* lung infections. The Company is also focused on the development of INS1009, an inhaled treprostinil prodrug. Treprostinil is a prostacyclin used in the treatment of pulmonary arterial hypertension (PAH), a chronic, life-threatening disorder characterized by abnormally high blood pressure in the arteries between the heart and lungs.

The Company was incorporated in the Commonwealth of Virginia on November 29, 1999. On December 1, 2010, the Company completed a business combination with Transave, Inc. (Transave), a privately held, New Jersey-based pharmaceutical company focused on the development of differentiated and innovative inhaled pharmaceuticals for the treatment of serious lung infections. The Company s continuing operations are based on the technology and products historically developed by Transave. The Company s principal executive offices are located in Bridgewater, New Jersey.

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 United States for complete consolidated financial statements have been condensed or are not included herein. The interim statements should be read in conjunction with the audited consolidated financial statements and notes thereto included in the Company s Form 10-K for the year ended December 31, 2014.

The results of operations of any interim period are not necessarily indicative of the results of operations for the full year. The unaudited interim condensed 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. The Company is responsible for the unaudited interim consolidated financial statements included in this report.

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

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, 2014:

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

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

- 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 U.S. treasuries and mutual funds listed in active markets.

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The Company s only assets and liabilities which were measured at fair value as of March 31, 2015 and December 31, 2014 were Level 1 and were comprised of cash and cash equivalents of $134.6 and $159.2 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 months ended March 31, 2015 and 2014, respectively.

As of March 31, 2015 and December 31, 2014, 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 Common Share - Basic net loss per common share is computed by dividing net loss by the weighted average number of common shares outstanding during the period. Diluted net loss per common share is computed by dividing net loss by the weighted average number of common shares and other dilutive securities outstanding during the period. Potentially dilutive securities from stock options, restricted stock units and warrants to purchase common stock would be antidilutive as the Company incurred a net loss. Potentially dilutive common shares resulting from the assumed exercise of outstanding stock options and warrants are determined based on the treasury stock method.

The following table sets forth the reconciliation of the weighted average number of shares used to compute basic and diluted net loss per share for the three months ended March 31, 2015 and 2014:

	2015	2014
	(In thousands, except per share amounts)	
Numerator:		
Net loss:	$ (27,369)	$ (14,298)
Denominator:		
Weighted average common shares used in calculation of basic net loss per share:	49,957	39,240
Effect of dilutive securities:		
Common stock options		
Restricted stock and restricted stock units		
Common stock warrant		
Weighted average common shares outstanding used in calculation of diluted net loss per share	49,957	39,240
Net loss per share:		
Basic and Diluted	$ (0.55)	$ (0.36)

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

	2015	2014
Stock options to purchase common stock	4,821	4,230
Restricted stock units	53	18

3. Identifiable Intangible Assets

The Company believes there are no indicators of impairment relating to its in-process research and development intangible assets as of March 31, 2015.

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4. Accrued Expenses

Accrued expenses consist of the following:

	As of March 31, 2015	As of December 31, 2014
	(in thousands)	
Accrued clinical trial expenses	$ 3,084	$ 2,113
Accrued technical operation expenses	835	762
Accrued construction costs	459	1,500
Accrued professional fees	898	542
Accrued interest payable	199	258
Other accrued expenses	501	146
	$ 5,976	$ 5,321

5. Debt

On June 29, 2012, the Company and its domestic subsidiaries, as co-borrowers, entered into a Loan and Security Agreement with Hercules Technology Growth Capital, Inc. (Hercules) that originally allowed the Company to borrow up to $20.0 million (Loan Agreement) at an interest rate of 9.25%. Most recently, on December 15, 2014, the Company and Hercules entered into a third amendment (the Third Amendment) to the Loan Agreement. In connection with the Third Amendment, the Company paid a commitment fee of $25,000, and at the closing, paid a facility fee of $125,000. Under the Third Amendment, the amount of borrowings was increased by $5.0 million to a total of $25.0 million and the interest-only period was extended through December 31, 2015. In addition, in the event the Company receives at least $90.0 million in cash proceeds from the completion of certain types of equity financings, subordinated debt financings, and/or up-front cash payments from corporate transactions prior to December 31, 2015, the Company has the option to extend the maturity date of the loan to January 1, 2018. If the Company elects to exercise such option, it must pay Hercules a $250,000 fee. The Company completed an equity financing in April 2015 in excess of $90.0 million (see Note 10 for more information).

The following table presents the components of the Company s debt balance as of March 31, 2015 (in thousands):

Debt:	
Notes payable	$ 25,000
Accretion of end of term charge	333
Issuance fees paid to lender	(231)
Discount from warrant	(113)
Current portion of long-term debt	(24,989)
Long-term debt	$

As of March 31, 2015, future principal repayments of the debt for each of the years ending December 31, 2015 and 2016 were as follows (in thousands):

Year Ending in December 31:		
2015	$	
2016 (due in full January 1, 2016)		25,000
	$	25,000

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

6. ***Shareholders Equity***

Common Stock As of March 31, 2015, the Company had 500,000,000 shares of common stock authorized with a par value of $0.01 and 50,001,770 shares of common stock issued and outstanding. In addition, as of March 31, 2015, the Company had reserved 4,821,435 shares of common stock for issuance upon the exercise of outstanding common stock options and 52,710 for issuance upon the vesting of restricted stock units.

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On August 18, 2014, the Company completed an underwritten public offering of 10,235,000 shares of the Company s common stock, which included the underwriter s exercise in full of its over-allotment option of 1,335,000 shares, at a price to the public of $11.25 per share. The Company s net proceeds from the sale of the shares, after deducting the underwriter s discount and offering expenses of $7.1 million, were $108.0 million. See Note 10 for the Subsequent Event related to the sale of additional shares in April 2015.

Preferred Stock As of March 31, 2015, 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 currently has one equity compensation plan, the 2013 Incentive Plan, which was approved by shareholders at the Company s Annual Meeting of Shareholders on May 23, 2013 (the 2013 Incentive Plan). The 2013 Incentive Plan is administered by the Compensation Committee and the Board of Directors of the Company. Under the terms of the 2013 Incentive Plan, the Company is authorized to grant a variety of incentive awards based on its common stock, including stock options (both incentive stock options and non-qualified stock options), performance options/shares and other stock awards, as well as the payment of incentive bonuses to all employees and non-employee directors. As of March 31, 2015, 58,886 shares of the Company s common stock were reserved for future grants (or issuances) of restricted stock, restricted stock units, stock options, and stock warrants under the 2013 Incentive Plan. The 2013 Incentive Plan will terminate on April 16, 2023 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. For the quarter ended March 31, 2015, the Company granted 200,000 inducement stock options 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 March 31,	
	2015	**2014**
Volatility	79%-82%	84%-86%
Risk-free interest rate	1.31%-1.57%	1.46%-1.76%
Dividend yield	0.0%	0.0%
Expected option term (in years)	6.25	6.25
Weighted-average fair value of stock options granted	$11.66	$14.35

For all periods presented, the volatility factor was based on the Company s historical volatility since the closing of the Company s merger with Transave on December 1, 2010. The expected life was determined using the simplified method as described in ASC Topic 718, Accounting for Stock Compensation , which is the midpoint between the vesting date and the end of the contractual term. The risk-free interest rate is based on the U.S. Treasury yield in effect at the date of grant. Forfeitures are based on actual percentage of option forfeitures since the closing of the

Company s merger with Transave on December 1, 2010, and this is the basis for future forfeiture expectations.

From time to time, the Company grants performance-condition options to certain of the Company s employees. Vesting of these options is subject to the Company achieving certain performance criteria established at the date of grant and the individuals fulfilling a service condition (continued employment). As of March 31, 2015 the Company had performance options totaling 193,334 shares outstanding which have not met the recognition criteria to date. For the three months ended March 31, 2015, approximately $1.5 million of non-cash compensation expense was recorded related to certain performance based options as the recognition criteria was met upon the marketing authorization application (MAA) for ARIKAYCE being accepted for filing by the European Medicines Agency (EMA) in February 2015.

The following table summarizes the Company s aggregate stock option activity for the three months ended March 31, 2015:

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	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life in Years	Aggregate Intrinsic Value (in thousands)
Options outstanding at December 31, 2014	4,400,106	$ 10.59		
Granted	619,150	$ 16.83		
Exercised	(178,071)	$ 8.28		
Forfeited or expired	(19,750)	$ 14.49		
Options outstanding at March 31, 2015	4,821,435	$ 11.46	8.19	$ 45,030
Vested and expected to vest at March 31, 2015	4,593,714	$ 11.33	8.17	$ 43,494
Exercisable at March 31, 2015	1,552,681	$ 8.25	7.72	$ 19,496

The total intrinsic value of stock options exercised during the three months ended March 31, 2015 and 2014 was $1.3 million and $0.6 million, respectively.

As of March 31, 2015, there was $25.6 million of unrecognized compensation expense related to unvested stock options which is expected to be recognized over a weighted average period of 2.6 years. Included above in unrecognized compensation expense was $1.5 million related to outstanding performance-based options. The following table summarizes the range of exercise prices and the number of stock options outstanding and exercisable:

	Outstanding as of March 31, 2015			Exercisable as of March 31, 2015	
Range of Exercise Prices	Number of Options	Weighted Average Remaining Contractual Term (in years)	Weighted Average Exercise Price	Number of Options	Weighted Average Exercise Price
3.03 3.29	180,188	6.75	3.05	131,810	3.04
3.40 3.40	708,314	7.45	3.40	442,697	3.40
3.60 6.90	605,545	7.70	6.02	327,413	5.91
6.96 12.44	885,025	7.65	11.05	358,377	11.09
12.58 12.58	577,550	8.39	12.58	25,000	12.58
12.66 14.65	483,800	8.77	13.91	84,000	14.13
14.81 16.07	583,650	9.38	15.96	28,175	15.62
16.19 20.49	779,363	8.77	19.49	151,458	19.59
21.09 21.21	3,000	9.97	21.17		
21.54 21.54	15,000	8.81	21.54	3,751	21.54

Restricted Stock and Restricted Stock Units The Company may grant Restricted Stock (RS) and Restricted Stock Units (RSUs) to eligible employees, including its executives, and non-employee directors. Each RS and RSU represents a right to receive one share of the Company s common stock upon the completion of a specific period of continued service or achievement of a certain milestone. RS and RSU awards granted are generally 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 three months ended March 31, 2015:

	Number of RSUs	Weighted Average Grant Price

Outstanding at December 31, 2014	20,502	$	19.47
Granted	49,776		16.07
Released	(17,568)		20.49
Outstanding at March 31, 2015	52,710	$	15.92
Expected to vest	52,710	$	15.92

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 months ended March 31, 2015 and 2014:

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	Three months ended March 31,	
	2015	2014
	(in millions)	
Research and development expenses	$ 1.3	$ 0.9
General and administrative expenses	3.2	1.5
Total	$ 4.5	$ 2.4

8. Income Taxes

The benefit for income taxes was $0 and $4.4 million for the three months ended March 31, 2015 and 2014, respectively. The benefit for income taxes recorded for the three months ended March 31, 2014 solely reflects the reversal of a valuation allowance previously recorded against the Company s New Jersey State net operating losses (NOL) that resulted from the Company s sale of a portion of its New Jersey State NOLs under the State of New Jersey s Technology Business Tax Certificate Transfer Program (the Program) for cash of $4.4 million, net of commissions. The Program allows qualified technology and biotechnology businesses in New Jersey to sell unused amounts of NOLs and defined research and development tax credits for cash.

The Company is subject to US federal and state income taxes. The Company has never been audited and the statute of limitations for tax audit is open for the federal tax returns for the years ended 2011 and later and is generally open for certain states for the years 2010 and later. However, except in 2009, the Company has incurred net operating losses since inception. Such loss carryforwards would be subject to audit in any tax year in which those losses are utilized, notwithstanding the year of origin. The Company s policy is to recognize interest accrued related to unrecognized tax benefits and penalties in income tax expense. The Company has recorded no such expense. As of March 31, 2015 and December 31, 2014, the Company has recorded no reserves for unrecognized income tax benefits, nor has it recorded any accrued interest or penalties related to uncertain tax positions. The Company does not anticipate any material changes in the amount of unrecognized tax positions over the next twelve months.

At December 31, 2014, the Company had federal net operating loss carryforwards for income tax purposes of approximately $461.8 million. Due to the limitation on NOLs as more fully discussed below, $283.5 million of the NOLs are available to offset future taxable income, if any. The NOL carryovers and general business tax credits expire in various years beginning in 2018. For state tax purposes, the Company has approximately $63 million of New Jersey NOLs available to offset against future taxable income or to be sold as part of the New Jersey Transfer Program. The Company also has California and Virginia NOLs that are entirely limited due to Section 382 (as discussed below), in addition to changing state apportionment allocations, as the Company is now 100% resident in New Jersey.

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

9. ***Commitments and Contingencies***

Commitments

The Company has an operating lease for office and laboratory space located in Bridgewater, NJ that terminates in November 2019. Future minimum rental payments under this lease are $3.4 million. The Company also leases office space in Richmond, VA, where the Company s corporate headquarters were previously located, through October 2016. Future minimum rental payments under this lease total approximately $0.8 million. During 2011, the Company recorded a net present value charge of $1.2 million in general and administrative expenses associated with vacating the Richmond facility. The remaining accrual for this charge was $0.4 million as of March 31, 2015. In December 2014, the Company entered into an agreement to sublet this space for the remainder of the lease term.

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Rent expense charged to operations was $0.2 million and $0.3 million for the three months ended March 31, 2015 and 2014, respectively. Future minimum rental payments required under the Company s operating leases for the period from April 1, 2015 to December 31, 2015 and for each of the next five years are as follows (in thousands):

Year Ending in December 31:		
2015 (remaining)	$	872
2016		1,144
2017		741
2018		762
2019		718
2020		
	$	4,237

Legal Proceedings

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

10. Subsequent Event

On April 6, 2015, the Company completed an underwritten public offering of 11,500,000 shares of the Company s common stock, which included the underwriter s exercise in full of its over-allotment option of 1,500,000 shares, at a price to the public of $20.65 per share. The Company s net proceeds from the sale of the shares, after deducting the underwriter s discount and offering expenses of $14.5 million, were approximately $223.0 million. As a result of the offering, the Company had 61,501,770 shares issued and outstanding immediately following the closing.

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

Forward-looking statements include, but are not limited to: failure or delay of European Medicines Agency, Health Canada, United States Food and Drug Administration and other regulatory reviews and approvals; competitive developments affecting the Company s product candidates; delays in product development or clinical trials or other studies; patent disputes and other intellectual property developments relating to the Company s product candidates; unexpected regulatory actions, delays or requests; the failure of clinical trials or other studies or results of clinical trials or other studies that do not meet expectations; the fact that subsequent analyses of clinical trial or study data may lead to different (including less favorable) interpretations of trial or study results or may identify important implications of a trial or study that are not reflected in Company s prior disclosures, and the fact that trial or study results or subsequent analyses may be subject to differing interpretations by regulatory agencies; the inability to successfully develop the Company s product candidates or receive necessary regulatory approvals; inability to make product candidates commercially successful; changes in anticipated expenses; changes in the Company s financing requirements or ability to raise additional capital; our ability to complete development of, receive regulatory approval for, and successfully commercialize ARIKAYCE or INS1009; our estimates of expenses and future revenues and profitability; our plans to develop and market new products and the timing of these development programs; our estimates of the size of the potential markets for our product candidates; our selection and licensing of product candidates; our ability to attract third parties with acceptable development, regulatory and commercialization expertise; the benefits to be derived from corporate license agreements and other third party efforts, including those relating to the development and commercialization of our product candidates; the degree of protection afforded to us by our intellectual property portfolio; the safety and efficacy of our product candidates; sources of revenues and anticipated revenues, including contributions from license agreements and other third party efforts for the development and commercialization of products; our ability to create an effective direct sales and marketing infrastructure for products we elect to market and sell directly; the rate and degree of market acceptance of our product candidates; the timing and amount of reimbursement for our product candidates; the success of other competing therapies that may become available; and the availability of adequate supply and manufacturing capacity and quality for our product candidates.

Forward-looking statements are based upon our current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause our actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timing discussed, projected, anticipated or indicated in any forward-looking statements. Such factors include, among others, the factors discussed in Item 1A Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2014 filed with the Securities and Exchange Commission (SEC) on February 27, 2015. We caution readers not to place undue reliance on any such forward-looking statements, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the Securities and Exchange Commission, to publicly update or revise any such statements to reflect any change in our expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

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, 2014.

OVERVIEW

Insmed is a biopharmaceutical company dedicated to improving the lives of patients battling serious and rare lung diseases. We are focused on the development and commercialization of ARIKAYCE, or liposomal amikacin for inhalation (LAI), for at least two identified orphan patient populations: patients with nontuberculous mycobacteria (NTM) lung infections and cystic fibrosis (CF) patients with *Pseudomonas aeruginosa (Pseudomonas)* lung infections. We are also focused on the development of INS1009, an inhaled treprostinil prodrug. Treprostinil is a prostacyclin used in the treatment of pulmonary arterial hypertension (PAH), a chronic, life-threatening disorder characterized by abnormally high blood pressure in the arteries between the heart and lungs.

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In March 2014, we reported top-line clinical results from the double-blind portion of our phase 2 clinical trial in the United States (US) and Canada of ARIKAYCE in patients who had treatment-resistant lung infections caused by NTM. The randomized, double-blind, placebo-controlled phase 2 clinical trial compared ARIKAYCE (590 mg delivered once daily), added to standard of care treatment, versus standard of care treatment plus placebo, in 90 adult patients with treatment resistant NTM lung disease. Eligibility for the study required patients to have been on the American Thoracic Society/Infectious Disease Society of America guideline therapy for at least six months prior to screening and to continue to have persistently positive mycobacterial cultures. The primary efficacy endpoint of the study was a semi-quantitative measurement of the change in mycobacterial density on a seven-point scale from baseline (day one) to the end of the randomized portion of the trial (day 84). ARIKAYCE did not meet the pre-specified level for statistical significance of the primary efficacy endpoint, although there was a positive trend (p=0.148) in favor of ARIKAYCE. A secondary efficacy endpoint of the study was proportion of subjects with culture conversion to negative. With regard to this secondary endpoint, 11 out of 44 patients treated with ARIKAYCE (added to standard of care treatment) demonstrated clearance of the infecting mycobacterial organism (culture negative) at day 84 of the study as compared to 3 out of 45 patients treated with placebo (added to standard of care treatment) (p=0.01).

In May 2014, additional data from the open-label portion of the phase 2 trial were presented in a poster session at the American Thoracic Society meeting. At the conclusion of the 84-day double blind phase of the trial, 78 of the 80 patients who completed the double-blind phase agreed to receive once-daily ARIKAYCE plus standard of care treatment for an additional 84 days. Data from 68 of the patients who completed the visits during the additional open-label phase were available for inclusion in the poster. The results collected from the open-label phase showed that 21 of these patients were culture negative for NTM at Day 168. These data reflect 10 patients who were culture negative at Day 84 as well as 5 additional patients from the ARIKAYCE arm and 6 additional patients who were initially on placebo and switched to ARIKAYCE during the open-label phase.

In June 2014, the US Food and Drug Administration (FDA) granted ARIKAYCE Breakthrough Therapy Designation for the treatment of adult patients with NTM lung disease who are treatment refractory. This designation is based on findings from our U.S. phase 2 clinical trial of ARIKAYCE to treat NTM lung infections. ARIKAYCE has already received Orphan Drug, Qualified Infectious Disease Product (QIDP) and Fast Track designations from the FDA for the treatment of NTM lung infections and has also received Orphan Drug Designation from the European Medicines Agency (EMA).

In the fourth quarter of 2014, we filed a Marketing Authorization Application (MAA) with the EMA for ARIKAYCE for the treatment of NTM lung infections as well as *Pseudomonas* lung infections in CF patients. The MAA for ARIKAYCE was validated in February 2015 after the EMA s pediatric committee approved the Pediatric Investigation Plan (PIP) for ARIKAYCE. The validation of the MAA filing is the start of the formal review process by the EMA.

In addition, following discussions with the FDA, we have commenced a phase 3 randomized, open-label, global clinical study that is designed to confirm the positive culture conversion results seen in our phase 2 clinical trial. This phase 3 study is investigating ARIKAYCE for use in non-CF patients 18 years and older with *Mycobacterium avium* complex (MAC) NTM lung infections who have thus far failed to achieve culture conversion on a multi-drug treatment regimen. This subgroup of patients in the phase 2 trial responded particularly well to treatment with ARIKAYCE. We believe this clinical trial will confirm the previous study results and could provide a path to filing and approval for an indication in patients with NTM who are refractory to treatment. Following discussions with the FDA, the primary efficacy endpoint will be the proportion of patients achieving culture conversion, with additional goals of demonstrating sustainability and safety. The protocol for the phase 3 trial was finalized following dialogue with the FDA and was approved by the U.S. Central Institutional Review Board (IRB). We initiated the global trial in early 2015 and expect to complete enrollment within one year. We anticipate having preliminary top-line clinical results from the phase 3 study in mid-2016. If the study meets the primary endpoint of culture conversion, we believe we would be eligible to submit a new drug application pursuant to 21 CFR 314 Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) which permits FDA to approve a drug based on a surrogate endpoint provided the sponsor commits to study the drug further to verify and describe the drug s clinical benefit. We expect to conduct the trial at over eighty sites including the United States, Europe, Australia, Japan and Canada with enrollment of approximately 300 patients.

In addition to ARIKAYCE, we believe that we can apply our proven design and development expertise to advance INS1009, an investigational sustained-release inhaled treprostinil prodrug that has the potential to address certain of the current limitations of existing inhaled prostanoid therapies in PAH. We believe that INS1009 may prolong duration of effect and may provide greater consistency in pulmonary arterial pressure reduction over time. Current inhaled prostanoid therapies must be dosed four to nine times per day. Reducing dose frequency therefore has the potential to ease patient burden and to positively impact compliance. Additionally, we believe that INS1009 over time may reduce side effects, including elevated heart rate, low blood pressure, and severity and/or frequency of cough, associated with high initial drug levels and local upper airway exposure when using current inhaled prostanoid therapies.

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In late 2014, we had a pre-investigational new drug (pre-IND) meeting with the FDA for INS1009 and clarified that, subject to final review of the pre-clinical 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 include full safety and effectiveness reports, but unlike a traditional NDA the applicant may rely at least in part on studies not conducted by or for the applicant. The ability to rely on existing data to support safety and/or effectiveness can reduce the time and cost associated with traditional NDAs. We are conducting preclinical work and toxicology evaluations related to the unique formulation and route of administration and if results from these studies support continued product development, we may continue advancing the program with the goal of submitting an investigational new drug (IND) application and commencing a phase 1 trial in the second half of 2015.

We also plan to develop, acquire, in-license or co-promote other products that address orphan or rare diseases possibly in the fields of pulmonology and infectious disease. Our current primary development focus is to obtain regulatory approval for ARIKAYCE in the U.S. for the NTM indication and in Europe for the NTM and CF indications, enroll and complete our global phase 3 NTM study, and prepare for commercialization, assuming regulatory approval in Europe, in the US, Canada and Japan. We anticipate that, if approved, ARIKAYCE would be the first once-a-day inhaled antibiotic treatment option available for the CF indication and the NTM indication in the US, Europe or Canada.

The following table summarizes the current status of ARIKAYCE and INS1009 development:

Product Candidate/Target Indications	**Status**	**Next Expected Milestones**
ARIKAYCE Non-tuberculous mycobacteria (NTM) lung infections	• We commenced a phase 3 global study (the 212 study) which is designed to confirm the positive culture conversion results seen in our phase 2 clinical trial. This phase 3 study is primarily investigating ARIKAYCE for use in the non CF, treatment failure population with MAC NTM lung infections. • We filed a MAA with the EMA, which was validated in February 2015. • We reported top line clinical results from our phase 2 clinical trial which stated that ARIKAYCE did not meet the pre specified level for statistical significance with respect to the primary endpoint, but demonstrated clearance of the infecting mycobacterial organism with regard to the secondary endpoint of culture conversion. • Granted Breakthrough Therapy designation by the FDA. • Granted Orphan Drug designation by the FDA and EMA.	• We expect to file a New Drug Submission (NDS) application with Health Canada during the second half of 2015 for the treatment of both NTM lung infections and *Pseudomonas* lung infections in CF patients. • We expect to complete enrollment in the 212 study in approximately twelve months from the initiation of the trial. • If approved, we expect ARIKAYCE would be the first approved inhaled antibiotic treatment in the US, Canada and Europe for NTM lung infections. • We are developing plans to commercialize ARIKAYCE, if approved, in certain countries in Europe, in the US, and Canada, and eventually Japan and certain other countries.

- Granted Qualified Infectious Disease Product (QIDP) designation, which includes Priority Review, by the FDA.

- Granted Fast Track designation by the FDA which permits a rolling submission of an NDA.

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ARIKAYCE *Pseudomonas aeruginosa* lung infections in CF patients	• We filed a MAA with the EMA, which was validated in February 2015. • We reported top line clinical results from our phase 3 clinical trial conducted in Europe and Canada, in which once daily ARIKAYCE achieved its primary endpoint of non-inferiority when compared to twice-daily tobramycin inhaled solution. • We are conducting a two year, open label safety study in patients who completed the phase 3 clinical trial. We expect to complete this study in mid-2015. • We reported top line results from the patients who completed the first year of the two year open label extension study. • Granted orphan drug designation by the EMA and FDA.	• We expect to file a NDS application with Health Canada during the second half of 2015 for the treatment of both NTM lung infections and *Pseudomonas* lung infections in CF patients. • We expect to announce final results from the two year open label extension study in the second half of 2015. • We are developing plans to commercialize ARIKAYCE, if approved, in certain countries in Europe and Canada where we expect it would be the only once a day treatment for Pseudomonas lung infections in CF patients. • We plan to initiate new studies in pediatric patients, however we currently do not plan to initiate any further studies in adult CF patients with *Pseudomonas* lung infections.
INS1009 (inhaled treprostinil prodrug) *for pulmonary arterial hypertension (PAH)*	• We completed a pre-IND meeting with the FDA for INS1009, and we have clarified that, subject to final review of the pre-clinical data, we could be eligible for a 505(b)(2) approval pathway.	• We expect to file an IND in the second half of 2015. • We expect to commence a phase 1 trial in the second half of 2015.

Our Strategy

Our strategy is to focus on the development and commercialization of innovative therapies for patients with serious lung diseases in orphan indications. While we believe that ARIKAYCE has the potential to treat many different diseases, our attention is initially focused on regulatory approval and commercialization preparation for our two initial indications: (1) NTM lung infections and (2) *Pseudomonas* lung infections in CF patients. Our current priorities are as follows:

- Continue conducting clinical trials to generate additional data supporting the safety and effectiveness of ARIKAYCE for the treatment of NTM lung infections and *Pseudomonas* lung infections in CF patients;

- Actively pursue approvals of ARIKAYCE to treat NTM lung infections through the submission of country-specific marketing authorizations to applicable regulatory bodies in the US, Europe, Canada, Japan and certain other countries;

- Actively pursue approval of ARIKAYCE to treat *Pseudomonas* lung infections in CF patients through the submission of marketing authorizations to applicable regulatory bodies in Europe and Canada;

- Expand our product supply chain in support of clinical development and if approved, commercialization;

- Prepare for commercial launch in the NTM indication in the US, Europe, Canada and eventually Japan and certain other countries;

- Prepare for commercial launch in *Pseudomonas* lung infections in CF patients indication in Europe and Canada;

- Attempt to develop, acquire, in-license or co-promote promising late stage or commercial products that we believe are complementary to ARIKAYCE and our core competencies; and

- Continue to develop novel formulations of existing therapies, where such reformulation could materially improve the treatment paradigm for the underlying disease, as we believe could be the case with INS1009 or enable pursuit of new indications.

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In support of these priorities, we completed our registrational phase 3 clinical study of ARIKAYCE in CF patients with *Pseudomonas* lung infections in Europe and Canada. We submitted regulatory marketing applications for the CF and NTM indications in Europe and expect to file in Canada in the second half of 2015. In the first half of 2014, we completed our US and Canadian phase 2 clinical study of ARIKAYCE for the treatment of NTM lung infections in treatment refractory patients. Following recent discussions with the FDA, we initiated a global phase 3 clinical trial of ARIKAYCE in NTM that will be a confirmatory study for patients with NTM lung infections who have thus far failed their multi-drug treatment regimen. We are scaling up manufacturing, we have identified certain second source suppliers, and we plan to implement supply and quality agreements in preparation for commercialization of ARIKAYCE. In February 2014, we entered into a contract manufacturing agreement with Therapure Biopharma Inc. (Therapure) for the manufacture of ARIKAYCE at the larger scales necessary to support commercialization. In July 2014, we entered into a commercialization agreement with PARI Pharma GmbH (PARI), the manufacturer of our drug delivery nebulizer, to address our commercial supply needs. We have commenced the build-out of our commercial infrastructure in preparation for potential commercial launches in Europe, Canada and the US. We completed a pre-IND meeting with the FDA for INS1009, our investigational inhaled treprostinil prodrug for use in the treatment of PAH and we have clarified that, subject to final review of the preclinical data, we would be eligible for a 505(b)(2) approval pathway. And finally, we will continue to evaluate opportunities for additional products through various business development channels.

Product Candidates

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

ARIKAYCE has the potential to be differentiated from amikacin and certain marketed drugs for the treatment of chronic lung infections if it can be demonstrated to provide improved efficacy, safety and patient convenience. We believe ARIKAYCE s ability to deliver high, sustained levels of amikacin directly to the lung and to the specific site of the underlying infection could distinguish it from other alternatives. We are also investigating ARIKAYCE s potential for durability of effect, benefiting patients when off treatment or for an extended period of treatment. In addition, the inhalation delivery of ARIKAYCE may reduce the potential for adverse events such as ototoxicity (hearing loss, ringing in the ears and/or loss of balance) and nephrotoxicity (toxicity to the kidneys), as compared with intravenous (IV) administration of amikacin. If approved, we expect that ARIKAYCE will be administered once-daily via inhalation using an ARIKAYCE specific eFlow® Nebulizer System. We believe that ARIKAYCE and the nebulizer system will reduce dosing frequency, as compared with the currently marketed inhaled antibiotics for CF indications, which require dosing two to three times daily with treatment times ranging from approximately 10 to 40 minutes per day. With once-daily administration we believe that ARIKAYCE can potentially improve patient compliance, which we believe may in turn lead to a reduction in the development of antibiotic resistance and, ultimately, lead to clinical and health economic benefits.

We believe that ARIKAYCE may provide: (i) improved efficacy resulting from sustained deposition of drug in the lung and improved ability to reach the site of infection (for CF *Pseudomonas* lung infections, this means penetration of biofilm and facilitated drug release by factors that are secreted by the bacteria, and for NTM, this means enhanced uptake into macrophages, targeting NTM within these cells); (ii) decreased adverse events and improved tolerability as compared with amikacin delivered intravenously, and (iii) reduced dosing frequency or treatment time as compared to existing inhaled products used by CF patients. In the future we may conduct head- to-head comparative studies that would be necessary to make comparative statements against other products.

Our second product candidate, INS1009, is an inhaled treprostinil prodrug that will address certain of the current limitations of inhaled prostanoid therapies in PAH. We believe that our inhaled treprostinil prodrug may prolong duration of effect and may provide greater consistency in pulmonary arterial pressure reduction over time. Current inhaled prostanoid therapies must be dosed four to nine times per day. Reducing dose frequency would therefore ease patient burden and may positively impact compliance. With a formulation where an active prostanoid is released over time, we believe the potential for side effects due to initially high drug levels and local upper airway exposure is reduced. For example, there may be reduced change in heart rate, change in blood pressure, and the severity and/or frequency of cough, as compared to treatment with current inhaled prostanoid therapies. Pulmonary hypertension was the 10th most expensive specialty therapy class in the United States in 2013 and approximately 25% of patients are non-adherent to medication therapy. We estimate the global market for pulmonary hypertension therapies to be approximately $4.5 billion, with the market for inhaled products representing approximately $500 million.

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ARIKAYCE for Patients with NTM Lung Infections

Overview of NTM Lung Infections

Nontuberculous mycobacteria, or NTM, are organisms common in soil and water that have been associated with lung disease in select patient groups. NTM have characteristics that are similar to tuberculosis, or TB, but NTM are not believed to be contagious. Many people have NTM in their bodies, but NTM do not normally lead to an infection, perhaps because the body s immune system successfully overcomes the threat of infection. It is not completely understood why certain individuals are susceptible to NTM infections. However, the patients who become infected by NTM often are immune-compromised, due to comorbidities such as HIV or immune-modulating treatments for rheumatoid arthritis, or have structural damage in their lungs, due to smoking, chronic obstructive pulmonary disease or CF, at the time of the infection.

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

Current Treatment Options and Limitations

Amikacin sulfate is a FDA-approved antibiotic with demonstrated efficacy in the treatment of a broad range of gram-negative infections. ARIKAYCE is in the aminoglycoside class of antibiotics. We believe there currently is no drug approved in the US, Europe or Canada for treatment of NTM lung infections, and as a result all current drug treatments for NTM are used off-label. Patients are often treated with the same antibiotics that are used to treat TB. Such treatments usually consist of lengthy multi-drug antibiotic regimens, which are often poorly tolerated and not very effective, especially in patients with severe disease and patients who have failed prior treatments. NTM patients average 7.6 antibiotic courses per year (SDI Healthcare Database, July 2009). Treatment guidelines published in 2007 in the *American Journal of Respiratory and Critical Care Medicine* reported that few clinical trials were under way to identify treatment recommendations, and no new antibiotics had been studied for the treatment of NTM lung infections in multi-center, randomized clinical trials since the late 1990s.

Although approved for other indications, amikacin sulfate is not approved by the FDA for NTM lung infections. In practice, however, it is often recommended by physicians as part of the multi-drug treatment regimen for some NTM patients. Amikacin is delivered most commonly by intravenous administration and, less often, by inhalation. Because the drug is delivered for months at a time, resulting in sustained high systemic (blood) levels of amikacin, there can be considerable toxicity, including ototoxicity and nephrotoxicity, associated with intravenous treatment. There are few prior studies to support what doses should be administered to effectively treat NTM patients even with these existing medications and they are often titrated on a patient by patient basis. If approved for NTM patients, we expect ARIKAYCE would be the first and only approved inhaled antibiotic for the treatment of NTM lung infections in the US, Europe or Canada.

Market

The prevalence of human disease attributable to NTM has increased over the past two decades. In 2012, in collaboration with the NIH, we funded a study performed by Clarity Pharma Research that showed there were an estimated 50,000 cases of pulmonary disease attributable to NTM in the US in 2011 and that such cases were estimated to be growing at a rate of 10% per year. NTM is four to five times more prevalent than TB in the US (Incidence of TB from Center for Disease Control and Prevention Morbidity and Mortality Weekly Report, March 2012). In a decade-long study, researchers found that the diagnosis of NTM in the US is increasing at approximately 8% per year and that those NTM patients over the age of 65 are 40% more likely to die than those who do not have the disease (Adjemian et al, Prevalence of Pulmonary Nontuberculous Mycobacterial Disease among Medicare Beneficiaries, USA, 1997-2007, American Journal of Respiratory and Critical Care Medicine, April 2012).

In 2013, we engaged Clarity Pharma Research to perform a similar chart audit study of NTM in Europe and Japan. Based on results of this study, researchers estimated that there are approximately 20,000 cases of pulmonary disease attributable to NTM within the European nations of France, Germany, the United Kingdom, Italy and Spain combined and approximately 30,000 in the 28 countries comprising the EU. In addition, there are nearly 32,000 cases in Japan. Although population-based data on the epidemiology of NTM infections in Europe are limited, consistent with US prevalence trends, recent published studies concur that prevalence in Europe is increasing and, according to a study published in the Japanese journal Kekkaku in 2011, Japan has one of the world s highest NTM disease rates.

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Although there are many species of NTM that have been reported to cause lung infections, ARIKAYCE is intended to treat two of the most common, *Mycobacterium avium* complex (MAC) and *Mycobacterium abscessus* (*M abscessus*). MAC accounts for the vast majority of NTM lung infections with prevalence rates from 72% to more than 85% in the US. The reported prevalence rates for *M. abscessus* range from 3% to 11% in the US. The diagnosed prevalence of NTM species causing lung infections varies geographically with MAC rates of 25% to 55% reported in Europe. MAC is also the most common NTM pathogen in Japan.

We are studying the economic and societal implications of NTM lung infections. We recently conducted a burden of illness study in the United States with a major medical benefits provider. This study has confirmed that NTM lung infections are costly to treat and manage. Active treatment of patients with NTM lung infection does result in significant medical expense savings as opposed to patients that are not treated. We plan to repeat this type of research globally in support of our overall disease awareness and education efforts.

ARIKAYCE for NTM Lung Infections: Potential Advantages and Distinguishing Features

If approved, we believe ARIKAYCE would be the first and only approved treatment in the US, Canada and Europe for patients battling NTM lung infections.

Liposomal Design and Formulation

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

Route of Administration

We believe ARIKAYCE has the potential to offer a safety profile different from that of intravenous delivery of amikacin. For example, unlike the intravenous administration of amikacin, ARIKAYCE would deliver the drug more directly to the site of disease. We anticipate this will result in less exposure of non-disease sites to amikacin. We believe this may reduce the potential for the occurrence of any drug-related systemic toxicity, such as nephrotoxicity, which is especially important with diseases like NTM that require long-term drug administration.

Anticipated Dosage Regimen

We believe ARIKAYCE, if approved, could improve patient convenience by providing once-a-day dosing. According to *SDI Healthcare Database* NTM patients average 7.6 antibiotic courses and 10.2 hospital days per year. We anticipate that ARIKAYCE will be administered once daily outside of the hospital until the NTM infection is eradicated and then for an additional period of one year, similar to the current multi-drug treatment guidelines. We believe that an effective inhaled treatment that improves the outcomes for an NTM patient would represent a significant benefit in the patient s quality of life.

Current Clinical Program

In the fourth quarter of 2014, we filed a MAA with the EMA for ARIKAYCE for the treatment of NTM lung infections as well as *Pseudomonas* lung infections in CF patients. The MAA for ARIKAYCE was validated in February 2015 after the EMA s pediatric committee approved the PIP for ARIKAYCE. The validation of the MAA filing is the start of the formal review process by the EMA.

In early 2015, following discussions with the FDA, we have commenced a phase 3 randomized, open-label, global study which is designed to confirm the positive culture conversion results seen in our phase 2 clinical trial. This confirmatory study is investigating ARIKAYCE for use in non-CF patients 18 years and older with MAC NTM lung infections who have thus far failed to achieve culture conversion on a multi-drug treatment regimen. This subgroup of patients in the phase 2 trial responded particularly well to treatment. We believe this approach will confirm the previous study results and provide a path to filing and approval for an indication in patients with NTM who are refractory to treatment. Following discussions with the FDA, the primary efficacy endpoint will be proportion of patients achieving culture conversion, with additional goals of demonstrating sustainability and safety. The protocol for the phase 3 trial was agreed upon following dialogue with the FDA and was approved by the U.S. Central IRB. We initiated the global trial in early 2015 and expect to complete enrollment within one year. We anticipate having preliminary top-line

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clinical results from the confirmatory phase 3 study in mid-2016. If the study meets the primary endpoint of culture conversion, we believe we would be eligible to submit a new drug approval application pursuant to 21 CFR 314 Subpart H (Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses) which permits FDA to approve a drug based on a surrogate endpoint provided the sponsor commits to study the drug further to verify and describe the drug s clinical benefit. We expect to conduct the trial at over eighty sites including the United States, Europe, Australia, Japan and Canada.

The 212 study is expected to enroll and randomize approximately 300 patients, with approximately 200 patients receiving ARIKAYCE once daily in addition to their current multi-drug treatment regimen and approximately 100 patients receiving only their current multi-drug treatment regimen. The primary efficacy endpoint in this open-label study will be proportion of patients achieving culture conversion by six months, which could allow for a NDA submission following data analysis. The definition of culture conversion is three consecutive monthly negative cultures. Patients in each arm who convert will continue their treatment for a total of twelve months from their first negative culture. Patients in each arm who do not convert have the option to continue in a follow-on study (the 312 follow-on study) for an additional twelve months of treatment with ARIKAYCE, in addition to the multi-drug regimen. The 312 follow-on study will be used to evaluate longer term safety of ARIKAYCE treatment.

In March 2014, we reported top-line clinical results from the double-blind portion of our phase 2 clinical trial in the US and Canada of ARIKAYCE in patients who have lung infections caused by NTM. The randomized, double-blind, placebo-controlled phase 2 clinical trial compared ARIKAYCE (590 mg delivered once daily), added to standard of care treatment, versus standard of care treatment plus placebo, in 90 adult patients with treatment resistant NTM lung disease. Eligibility for the study required patients to have been on the American Thoracic Society/Infectious Disease Society of America guideline therapy for at least six months prior to screening and to continue to have persistently positive mycobacterial cultures. The primary efficacy endpoint of the study was a semi-quantitative measurement of the change in mycobacterial density on a seven-point scale from baseline (day one) to the end of the randomized portion of the trial (day 84). ARIKAYCE did not meet the pre-specified level for statistical significance of the primary endpoint, although there was a positive trend in favor of ARIKAYCE. A secondary efficacy endpoint of the study was proportion of subjects with culture conversion to negative. With regard to this secondary endpoint, 11 out of 44 patients treated with ARIKAYCE (added to standard of care treatment) demonstrated negative cultures at day 84 of the study as compared to 3 out of 45 patients treated with placebo (added to standard of care treatment).

In May 2014, additional data from the open-label portion of the phase 2 trial were presented in a poster session at the American Thoracic Society meeting. At the conclusion of the 84-day double blind phase of the trial, 78 of the 80 patients completing the double-blind phase agreed to receive once-daily ARIKAYCE plus standard of care treatment for an additional 84 days. Data from 68 of these patients who completed the visits during the additional open label phase were available for inclusion in the poster. The results collected from the open label phase show that 21 of these patients were culture negative for NTM at Day 168. These data reflect 10 patients who were culture negative at Day 84 as well as 5 additional patients from the ARIKAYCE arm and 6 additional patients who were initially on placebo and switched to ARIKAYCE during the open-label phase. Additionally, we conducted a separate scintigraphy sub-study to examine drug deposition and distribution of ARIKAYCE in the lung with the PARI nebulizer.

In June 2014, the FDA granted ARIKAYCE Breakthrough Therapy Designation for the treatment of adult patients with NTM lung disease who are treatment refractory. This designation is based on findings from our U.S. phase 2 clinical trial of ARIKAYCE to treat NTM lung infections. ARIKAYCE has already received Orphan Drug, Qualified Infectious Disease Product (QIDP) and Fast Track designations from the FDA for the treatment of NTM lung infections and recently received Orphan Drug Designation from the EMA.

Development History

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

Data obtained from *in vitro* testing of ARIKAYCE with respect to four different strains of MAC and *M. abscessus* indicate dose response with ARIKAYCE and superior activity to amikacin in solution. We believe that the safety and efficacy data obtained from the phase 2 study in NTM patients, the phase 3, phase 2 and open label studies of ARIKAYCE in CF, the phase 2 study in non-CF patients with chronic lung disease and pulmonary infections, and the non-clinical data collected to date serve as the basis for further development of ARIKAYCE in patients with NTM lung infections.

In 2011, we submitted an IND to launch a phase 3 study of ARIKAYCE in CF and non-CF patients for the treatment of NTM lung infections in treatment refractory patients. In August 2011, prior to starting the NTM study, we announced that the FDA placed a clinical hold on our phase 3 trial. The clinical hold for the NTM study was lifted in January 2012. The FDA based its clinical hold decision on an initial review of the results of a long-term rat inhalation carcinogenicity study with ARIKAYCE. When rats were given

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ARIKAYCE daily by inhalation for two years, 2 of the 120 rats receiving the highest dose developed lung tumors. These rats received ARIKAYCE doses that were within two-fold of those in clinical studies (normalized on a body surface area basis or a lung weight basis). ARIKAYCE was not associated with changes that may lead to tumors in shorter-term studies in animals. Additionally, ARIKAYCE was not shown to be genotoxic in our standard series of tests. The relevance of the observed rat tumors to the use of ARIKAYCE in humans is not known. The FDA requested we conduct a phase 2 clinical trial, instead of our previously agreed upon phase 3 clinical trial in adult NTM patients, to provide proof-of-concept efficacy and safety data for ARIKAYCE in NTM patients. Despite the change in status from phase 3 to phase 2, the study design and target enrollment did not change. In connection with the FDA s decision to lift the clinical hold for all disease indications, we agreed to conduct a dog inhalation toxicity study of ARIKAYCE. In 2013, we concluded the dog inhalation toxicity study. In summary, the final report from the study stated that the lung macrophage response in dogs was similar to that seen in our previous 3 month dosing dog study, and there was no evidence of neoplasia, squamous metaplasia or proliferative changes.

Strategy for Commercialization

We currently plan to retain marketing rights for ARIKAYCE for the NTM indication. Given the current lack of approved treatments for NTM lung infections, we believe we will have a rapid and strong market position if ARIKAYCE is approved for commercialization in the NTM indication. We believe ARIKAYCE will require a limited commercial infrastructure because of the small focused nature of the potential physician prescribing population for NTM patients. We have commenced preparations for the potential commercialization of ARIKAYCE and we have filled several positions to support our future sales, market access and marketing efforts. We may also seek to out-license ARIKAYCE in certain countries in Europe, as well as outside of Europe, Canada and the US. We estimate the potential global market for NTM therapies could be approximately $1 billion.

ARIKAYCE for CF Patients with *Pseudomonas* Lung Infections

Overview of CF and Pseudomonas Lung Infections

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

Despite extensive treatment with multiple antibiotics, improved nutrition, and other treatments, life expectancy of a CF patient is only 38-40 years (Cystic Fibrosis Foundation Patient Registry, 2012). Median predicted age of survival is calculated using life table analysis (as calculated by actuaries) given the ages of the patients in the registry and the distribution of deaths. Using this calculation, half of the people in the patient registry are expected to live beyond the median predicted survival age, and half are expected to live less than the median predicted survival age.

Among other issues, CF causes thick, sticky mucus to develop in and clog the lungs. This creates an ideal environment for various pathogens, such as *Pseudomonas*, to colonize and lead to chronic infection of the lung, inflammation and progressive loss of lung function. In fact, chronic bronchial infections with *Pseudomonas* are a major cause of morbidity and mortality among patients with CF. Once a CF patient acquires a *Pseudomonas* infection, it is difficult to eradicate. The current, best available treatment is chronic administration of antibiotics to suppress the

bacteria, reduce inflammation and preserve lung function for as long as possible. The rate of infection with *Pseudomonas* in CF patients increases with age. It is estimated that 80% of adult CF patients have chronic infection due to *Pseudomonas* (Pritt et al, *Mucoid Pseudomonas in Cystic Fibrosis*, American Journal of Clinical Pathology, 2007). A study reported in the *Journal of Cystic Fibrosis* (Liou, 2010) found that deterioration in lung function of CF patients is the main cause of death and that, despite best efforts, lung function declines by 1% to 3% annually.

Current Treatment Options and Limitations

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

Antibiotics delivered via inhalation are part of the standard treatment for CF patients with *Pseudomonas* lung infections and are generally thought to be a way to deliver more active drug directly to the site of infection compared with other routes of administration. The most used treatment in the US for the management of chronic *Pseudomonas* infection in subjects with CF is

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

Market

We estimate that the global market for the treatment of *Pseudomonas* lung infections in CF patients is approximately $400 million. We believe this market is being driven by physicians desire to maintain the lung function of CF patients, which continues to decline in many patients despite extensive treatment with current therapies including currently approved inhaled antibiotics. We believe that the following additional factors may lead to further market growth:

- Better patient adherence to physician prescribed regimens resulting from more convenient (less frequent and less time consuming) treatments;

- Physicians initiating treatment with inhaled antibiotics earlier for patients with *Pseudomonas* in their lungs;

- CF patients living longer;

- Physicians moving to a different antibiotic every other month as opposed to giving patients off-treatment holidays on alternate months; and

- The standard of care in the rest of the world continuing to advance closer to that in the EU and the US.

ARIKAYCE for CF Patients with Pseudomonas Lung Infections: Potential Advantages and Distinguishing Features

Patient Compliance Considerations

We believe ARIKAYCE may facilitate better patient compliance with prescribed treatment regimens; patient compliance with or adherence to prescribed treatment is generally expected to impact the effectiveness of treatment. If a product can improve adherence, it may be able to differentiate itself from other marketed drugs. In the case of treatment and management of chronic *Pseudomonas* lung infections in CF patients, currently the most used treatment in the US is suppressive therapy with 300 mg twice daily of Tobi inhaled solution and 112 mg twice daily tobramycin inhaled powder. Tobi is administered twice daily for 28 days followed by a 28-day-off period. This cycle of on and off treatment is repeated in a chronic pattern. We anticipate that ARIKAYCE would be administered once daily for 28 days followed by a 28-day off-drug period. We believe that any inhaled treatment that reduces the treatment burden on a CF patient could represent a significant improvement in the patient s quality of life and result in improved compliance, as well as reduce the development of antibiotic resistance.

Liposomal Design and Formulation

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

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site of the *Pseudomonas* infection in CF patients lungs more efficiently than the other currently available aminoglycoside antibiotics, including currently available inhaled antibiotics.

In addition, ARIKAYCE has demonstrated a prolonged half-life in animals lungs. We believe this effect is due to our proprietary liposomal technology. One important measure of the effectiveness of antibiotics is the maintenance of anti-bacterial drug levels in the lung above the minimum inhibitory concentration. We anticipate that ARIKAYCE will be maintained in the human lung in a manner similar to what was demonstrated in animal studies.

We believe ARIKAYCE may be further differentiated from other marketed drugs for the treatment of chronic *Pseudomonas* lung infections in CF patients due to improved lung function during both on-treatment and off-treatment cycles. Typically an inhaled antibiotic is given to CF patients with chronic *Pseudomonas* lung infections for 28 days followed by a 28-day off-treatment cycle, which is often repeated chronically or for the rest of a patient s life. In February 2014, we reported interim data from our two-year open label extension study which showed a mean increase in relative change in FEV1 which was sustained during both on-treatment and off-treatment months. In addition, during phase 2 studies ARIKAYCE demonstrated statistically significant and clinically meaningful improvement in pulmonary function throughout the 28-day treatment period, and such improvement was sustained during the 28-days off treatment period.

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

Route of Administration

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

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

- Drug Resistance. High-level multi-drug resistance complicates eradication of such strains from the bronchial secretions of CF patients. *Pseudomonas* lung infections are commonly treated using aminoglycoside antimicrobial agents, such as amikacin and tobramycin. However, due to drug resistance, significantly higher concentrations of these drugs above the minimum inhibitory concentration are required at the site of infection. The intravenous dosage levels required to achieve such exposures can be nephrotoxic and ototoxic.

- Limited Penetration. There is limited penetration into and through the sputum/biofilm matrix by aminoglycoside antibiotics. The antibiotics are positively charged and the biofilm is negatively charged. As a result, the antibiotics bind to the biofilm and the availability of the drug at the location of the microorganism is suboptimal. We believe that our proprietary liposomal technology will result in localized targeting of drugs, leading to increased availability of the drug at the location of the microorganism, while significantly reducing drug exposure at non-disease sites throughout the body and reducing the occurrence of systemic drug-related toxicity.

Current Clinical Program

In the fourth quarter of 2014, we filed a MAA with the EMA for ARIKAYCE for the treatment of NTM lung infections as well as *Pseudomonas* lung infections in CF patients. The MAA for ARIKAYCE was validated in February 2015 after the EMA s pediatric committee approved the PIP for ARIKAYCE. The validation of the MAA filing is the start of the formal review process by the EMA.

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We completed a registrational phase 3 clinical trial of ARIKAYCE for CF patients with *Pseudomonas* lung infections in Europe and Canada during the second quarter of 2013. The phase 3 trial was a randomized, open label, multi-center study designed to assess the comparative safety and efficacy of once-daily ARIKAYCE administered for approximately 13 minutes via the eFlow Nebulizer System and twice-daily Tobi (tobramycin inhalation solution) administered for approximately 15 minutes per treatment via the PARI LC Plus Nebulizer System for a daily total of approximately 30 minutes per day in CF patients with *Pseudomonas*. A total of 302 adult and pediatric CF patients with chronic *Pseudomonas* were randomized to receive 28- days of ARIKAYCE treatment or Tobi delivered twice-daily via the PARI LC Plus® Nebulizer System over a 24-week treatment period. The primary endpoint of the study was relative change in FEV1 measured after three treatment cycles, with each cycle consisting of 28 days on treatment and 28 days off treatment. The study was designed to demonstrate non-inferiority to Tobi at a 5% non-inferiority margin with 80% power agreed upon by us and the EMA. Secondary endpoints measured were relative changes in FEV1 at other time points, time to and number of pulmonary exacerbations, time to antibiotic rescue treatment, change in density of *Pseudomonas* in sputum, respiratory hospitalizations and changes in Patient Reported Outcomes assessing Quality of Life. Top-line results from this study indicated:

- ARIKAYCE achieved its primary endpoint of non-inferiority to Tobi for relative change in FEV1 from baseline to the end of the study;

- Overall, secondary endpoints, as summarized above, showed comparability of once-daily ARIKAYCE compared with twice-daily Tobi; and

- The safety profile of ARIKAYCE was comparable to Tobi during all three treatment cycles, with adverse events consistent with those seen in similar studies and expected in a population of CF patients receiving inhaled antibiotics. There was no difference between arms in the reporting of serious adverse events and there were no unexpected adverse events.

We are conducting a two-year, open label safety study in patients that also completed our registrational phase 3 clinical study of ARIKAYCE for CF patients with *Pseudomonas* lung infections in Europe and Canada. Approximately 75% of the eligible patients that completed our registrational phase 3 clinical study consented to participate in the safety study. The patients in this study will receive ARIKAYCE for up to an additional two year period, using the same cycles of a 28 day on-treatment period and a 28 day off-treatment period. In February 2014, we reported interim data from our two-year open label extension study which showed a mean increase in relative change in FEV1 which was sustained during both on-treatment and off-treatment months. These interim data were included in our regulatory filings with the EMA, which we filed in December 2014 and we plan to include these data in our filings with Health Canada, which we expect to submit in the second half of 2015. We expect to complete this study in mid-2015.

ARIKAYCE has been granted orphan drug status in the US and Europe for the treatment of *Pseudomonas* lung infections in CF patients.

Development History

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

- High concentrations of drug are deposited in the lung, and high levels are maintained for prolonged periods, with low serum concentrations;

- ARIKAYCE penetrates CF sputum and *Pseudomonas* biofilm;

- ARIKAYCE exhibits antipseudomonal activity in *in vitro* and *in vivo* models, including against resistant isolates; and

- Virulence factors secreted by *Pseudomonas* facilitate the release of amikacin from ARIKAYCE.

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

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

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

In connection with the FDA s decision to lift the clinical hold for the CF *Pseudomonas aeruginosa* lung infection indication, we agreed to conduct a 9 month dog inhalation toxicity study of ARIKAYCE. In 2013, we concluded the 9 month dog inhalation toxicity study. In summary, the final report from the study stated that the lung macrophage response in dogs was similar to that seen in our previous 3 month dosing study in dogs, and there was no evidence of neoplasia, squamous metaplasia or proliferative changes.

We currently do not plan to initiate any further studies in *Pseudomonas* lung infections, except for our pediatric commitments.

Strategy for Commercialization

We believe ARIKAYCE will require a limited commercial infrastructure because of the center-based approach most widely used in the care of CF patients worldwide. We may seek to out-license ARIKAYCE in certain countries in Europe, as well as outside of Europe, Canada and the US.

INS1009 Inhaled Treprostinil for Pulmonary Arterial Hypertension

Disease

Pulmonary Arterial Hypertension, or PAH, is a chronic, life-threatening disorder characterized by abnormally high blood pressure in the arteries between the heart and lungs of an affected individual. PAH is one form of pulmonary hypertension. Pulmonary arteries carry blood from the heart to the lungs, where it picks up oxygen to be delivered throughout the body. In PAH, the pulmonary arteries constrict abnormally. This forces the heart to pump harder to maintain adequate blood flow which causes blood pressure within the lungs to rise. Common early symptoms include shortness of breath, fatigue, weakness, chest pain, and fainting, particularly during physical activity. PAH worsens over time and is life-threatening because the pressure in a patient s pulmonary arteries rises to dangerously high levels, putting a strain on the heart leading to heart failure.

Market and Current Treatment Options

There is no cure for PAH. PAH is estimated to have a prevalence of between 15 and 50 cases per 1 million adults and is considered an orphan disease.

Several medications are used to treat PAH:

- Non-specific treatments such as anticoagulants, diuretics, and oxygen may be used. These drugs are not specifically approved for the treatment of PAH, but are commonly utilized. In specific circumstances, drugs such as digoxin or calcium channel blockers may also be used to treat PAH.

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- Several drugs have been approved specifically for the treatment of PAH. These drugs address three target pathophysiologic pathways: the endothelin pathway, the nitric oxide pathway, and the prostacyclin pathway. They may be used alone or in combination.

The long term outcomes of medically treated patients remain uncertain, and transplantation remains an option for patients who fail on drug therapy. Prostanoid formulations used to treat PAH include intravenous epoprostenol (prostacyclin), intravenous treprostinil (a prostacyclin analog), subcutaneous treprostinil, inhaled treprostinil, oral treprostinil and inhaled iloprost. All prostanoid compounds have the limitation of a short half-life in the body, including treprostinil.

For subcutaneous or intravenous administered treprostinil, continuous infusion is required and patients often experience injection site pain and increased risk of infection, respectively. Oral and inhaled forms of treprostinil require multiple dosing sessions per day with high and low cycling in blood levels. The initial high levels of drug and the local delivery of the drug may cause tolerability issues (cough, laryngeal irritation, emesis, hypotension and headache) and at the subsequent low levels of drug there may be reduced therapeutic benefit, especially in the overnight hours.

The current market for prostanoid therapies for PAH, including oral, IV and inhaled products, is in excess of $1 billion.

Current Program

INS1009. We believe that we can apply our proven design and development expertise to advance a new inhaled treatment that will address the current limitations of inhaled prostanoid therapies in PAH. We believe that our sustained-release inhaled treprostinil prodrug may prolong duration of effect and may provide greater consistency in pulmonary arterial pressure reduction over time. Current inhaled prostanoid therapies must be dosed four to nine times per day. Reducing dose frequency would therefore ease patient burden and may positively impact compliance. With our inhaled treprostinil prodrug that is released over time, we believe the potential for side effects due to initially high drug levels and local upper airway exposure is reduced. For example, there may be reduced change in heart rate, change in blood pressure, and the severity and/or frequency of cough, as compared to treatment with current inhaled prostanoid therapies.

In late 2014, we completed a pre-IND meeting with the FDA for INS1009 and clarified that, subject to final review of the pre-clinical data, INS1009 could be eligible for a Section 505(b)(2) approval pathway. We are conducting preclinical work and toxicology evaluations related to the unique formulation and route of administration and, if results from these studies support our product concept, we may continue the program into development with the goal of submitting an IND application and commencing a phase 1 clinical study in the second half of 2015.

Strategy for Commercialization

We are constructing our development and commercialization plan for INS1009. We will evaluate independent development, co-development and out-licensing alternatives, as well as similar commercialization approaches.

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

Overview of Non-CF Bronchiectasis and Pseudomonas Lung Infections

Based on the positive results of a phase 2 placebo-controlled study in non-CF bronchiectasis, we believe ARIKAYCE has the potential to be used to treat non-CF bronchiectasis characterized by *Pseudomonas* lung infections. However, we are currently concentrating our development efforts on the treatment of patients with NTM lung infections and *Pseudomonas* lung infections in CF patients.

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

Market

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

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for this indication. When bronchiectasis patients become infected with *Pseudomonas*, they tend to have more frequent exacerbations and hospitalizations and are more frequent users of antibiotics.

Development Program

ARIKAYCE has been granted orphan drug status in the US for the treatment of bronchiectasis in patients with *Pseudomonas* and other susceptible microbial pathogens.

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

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

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

Although we believe there is an opportunity to develop ARIKAYCE for non- CF bronchiectasis, we currently do not intend to initiate further clinical studies with respect to a non-CF bronchiectasis indication.

KEY COMPONENTS OF OUR STATEMENT OF OPERATIONS

Revenues

We currently do not recognize any revenue from product sales or other sources.

Research and Development Expenses

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

Since 2011, we have focused our development activities principally on our proprietary, advanced liposomal technology designed specifically for inhalation lung delivery. In 2013, we completed a phase 3 trial in Europe and Canada in which we evaluated ARIKAYCE in CF patients with Pseudomonas lung infections. In 2014, we completed a phase 2 clinical trial in the US and Canada of ARIKAYCE in patients with NTM lung infections. In 2015, we commenced a global phase 3 trial for ARIKAYCE for patients with NTM lung infections. We are also conducting an open label extension study in which CF patients that completed our phase 3 trial receive ARIKAYCE for a period of two years. Since our business combination with Transave, the majority of our research and

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development expenses have been for our ARIKAYCE program. Our development efforts in 2015 principally relate to the development of ARIKAYCE in the NTM indication and, to a lesser extent, for INS1009 for PAH.

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

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

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

General and Administrative Expenses

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

product candidates, specifically in Europe.

Debt Issuance Costs

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

Investment Income and Interest Expense

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

RESULTS OF OPERATIONS

Comparison of the Three Months Ended March 31, 2015 and 2014

Net Loss

Net loss for the quarter ended March 31, 2015 was $27.4 million, or ($0.55) per common share basic and diluted, compared with a net loss of $14.3 million, or ($0.36) per common share basic and diluted, for the quarter ended March 31, 2014. The

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$13.1 million increase in our net loss in the quarter ended March 31, 2015 as compared to the same period in 2014 was primarily due an increase in 2015 expenses including a:

- $5.8 million increase in our research and development expenses that primarily resulted from an increase in clinical trial expenses related to the 212 global study in the first quarter of 2015, an increase in manufacturing expenses as a result of the build-out of a production area at Therapure s facility, and an increase in internal expenses, specifically compensation and related expenses; and

- $2.8 million increase in our general and administrative expenses resulted from an increase in certain administrative expenses, primarily an increase in noncash stock-based compensation related to the vesting of certain performance-based stock options.

In addition, the quarter ended March 31, 2014 included a $4.4 million benefit from income taxes resulting from the sale of a portion of our New Jersey State NOLs under the State of New Jersey s Technology Business Tax Certificate Transfer Program for cash, net of commissions. The reason for the decrease in tax benefit in 2015 was due to timing, as we recognized the full tax benefits of the 2014 sales of NOLs in calendar year 2014, while the 2013 sales of NOLs were recognized in the first quarter of 2014.

Research and Development Expenses

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

	Quarters Ended March 31,		Increase	
	2015	2014	$	%
External Expenses				
Clinical development & research	$ 5,883	$ 3,084	$ 2,799	90.8%
Manufacturing	4,352	2,861	1,491	52.1%
Regulatory and quality assurance	627	493	134	27.2%
Subtotal external expenses	$ 10,862	$ 6,438	$ 4,424	68.7%
Internal Expenses				
Compensation and related expenses	$ 4,770	$ 4,012	$ 758	18.9%
Other internal operating expenses	1,532	901	631	70.0%
Subtotal internal expenses	$ 6,302	$ 4,913	$ 1,389	28.3%
Total	$ 17,164	$ 11,351	$ 5,813	51.2%

Research and development expenses increased to $17.2 million during the quarter ended March 31, 2015 from $11.4 million in the same period in 2014. The $5.8 million increase was primarily due to a $2.8 million increase in external clinical development and research expenses, primarily related to clinical trial expenses related to the 212 global study, a $1.5 million increase in manufacturing expenses as a result of the build-out of a production area at Therapure s facility, and a $1.4 million increase in internal expenses, specifically a $0.8 million increase in compensation and related expenses. We expect research and development expenses to increase in 2015 as compared to 2014 due primarily to the clinical trial activity related to the 212 study and also for research expenses related to our INS1009 program for PAH.

General and Administrative Expenses

General and administrative expenses for the quarters ended March 31, 2015 and 2014 comprised the following:

	Quarters Ended March 31,		Increase	
	2015	2014	$	%
General & administrative	$ 7,766	$ 5,285	$ 2,481	46.9%
Pre-commercial expenses	1,776	1,443	333	23.1%
Total general & administrative expenses	$ 9,542	$ 6,728	$ 2,814	41.8%

General and administrative expenses increased to $9.5 million during the quarter ended March 31, 2015 from $6.7 million in the same period in 2014. The $2.8 million increase was primarily due to a $1.5 million increase in noncash stock-based compensation expense related to certain performance based stock options as the recognition criteria was met upon the marketing authorization application (MAA) for ARIKAYCE being accepted for filing by the European Medicines Agency (EMA) in February 2015 and

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an increase in administrative and pre-commercial expenses. We expect general and administrative expenses to increase in 2015 as compared to 2014 due, in part, to an increase in expenditures related to commercial readiness activities in certain European markets.

Interest Expense

Interest expense was $0.7 million during the quarter ended March 31, 2015 as compared to $0.6 million in the same period in 2014. The increase in interest expense in 2015 relates to an increase in our borrowings from Hercules. In December 2014, we entered into a third amendment to the Loan and Security Agreement with Hercules which increased our borrowings $5.0 million to a total of $25.0 million.

Benefit from Income Taxes

The benefit for income taxes was $0 and $4.4 million for the quarters ended March 31, 2015 and 2014, respectively. The benefit for income taxes recorded for the quarter ended March 31, 2014 solely reflects the reversal of a valuation allowance previously recorded against our New Jersey State net operating losses (NOLs) that resulted from the sale of a portion of our New Jersey State NOLs under the State of New Jersey s Technology Business Tax Certificate Transfer Program (the Program) for cash of $4.4 million, net of commissions. The Program allows qualified technology and biotechnology businesses in New Jersey to sell unused amounts of NOLs and defined research and development tax credits for cash. The reason for the decrease in tax benefit in 2015 was due to timing, as we recognized the full tax benefits of the 2014 sales of NOLs in calendar year 2014, while the 2013 sales of NOLs were recognized in the first quarter of 2014.

LIQUIDITY AND CAPITAL RESOURCES

Overview

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

We believe we currently have sufficient funds to meet our financial needs in 2015. We may opportunistically raise additional capital and may do so through equity or debt financing(s), strategic transactions or otherwise. Such additional funding may be necessary to continue to develop our potential product candidates, to pursue the license or purchase of other technologies, to commercialize our product candidates or to purchase other products. We cannot assure you that adequate capital will be available on favorable terms, or at all, when needed. If we are unable to obtain sufficient additional funds when required, we may be forced to delay, restrict or eliminate all or a portion of our research or development programs, dispose of assets or technology or cease operations. During 2015 we plan to continue to fund further clinical development of ARIKAYCE and INS1009, invest in third-party manufacturing capacity, support efforts to obtain regulatory approvals and prepare for commercialization in certain European countries. Our cash requirements in 2015 will be impacted by a number of factors, the most significant of

which, being the enrollment rates and other expenses related to the 212 study.

On April 6, 2015, we completed an underwritten public offering of 11.5 million shares of our common stock, which included the underwriter s exercise in full of its over-allotment option of 1.5 million shares, at a price to the public of $20.65 per share. Our net proceeds from the sale of the shares, after deducting the underwriter s discount and offering expenses of $14.5 million, were $223.0 million.

Cash Flows

As of March 31, 2015, we had total cash and cash equivalents of $134.6 million, as compared with $159.2 million as of December 31, 2014. The $24.6 million decrease was due primarily to the use of cash in operating activities. Our working capital was $99.1 million as of March 31, 2015.

Net cash used in operating activities was $24.9 million and $12.6 million for the quarters ended March 31, 2015 and 2014, respectively. Excluding the cash proceeds from the sale of a portion of our New Jersey State NOLs under the State of New Jersey s Technology Business Tax Certificate Transfer Program of $4.4 million in 2014, net cash used in operating activities in 2015 and 2014

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would have been $24.9 million and $17.0 million, respectively. The net cash used in operating activities during 2015 and 2014 was primarily for the clinical, regulatory and pre-commercial development of ARIKAYCE.

Net cash used in investing activities was $1.3 million and $0.3 million for the quarters ended March 31, 2015 and 2014, respectively. The net cash used in investing activities in 2015 primarily related to payments for the build out of our headquarters and lab facility in Bridgewater, New Jersey.

Net cash provided by financing activities was $1.5 million and $0.3 million for the quarters ended March 31, 2015 and 2014, respectively. Net cash provided by financing activities in 2015 and 2014 were proceeds received from stock option exercises.

Contractual Obligations

On June 29, 2012, we and our domestic subsidiaries, as co-borrowers, entered into a Loan and Security Agreement with Hercules that allowed us to borrow up $20.0 million (Loan Agreement) at an interest rate of 9.25%. Most recently on December 15, 2014, we entered into a third amendment (the Third Amendment) to the Loan Agreement with Hercules. In connection with the Third Amendment, we paid a commitment fee of $25,000, and at the closing, paid a facility fee of $125,000. Under the Third Amendment, the amount of borrowings was increased by $5.0 million to a total of $25.0 million and the interest-only period was extended through December 31, 2015. In addition, in the event we receive at least $90.0 million in cash proceeds from the completion of certain types of equity financings, subordinated debt financings, and/or up-front cash payments from corporate transactions prior to December 31, 2015, we have the option to extend the maturity date of the loan to January 1, 2018. If we elect to exercise the option, we are required to pay Hercules a $250,000 fee. We completed an equity financing in April 2015 which was in excess of $90.0 million.

We have an operating lease for office and laboratory space located in Bridgewater, New Jersey that expires in November 2019. Future minimum rental payments under this lease total approximately $3.4 million. We continue to lease office space in Richmond, Virginia where our corporate headquarters was previously located. Future minimum rental payments under this lease total approximately $0.8 million. During 2011, we recorded a net present value charge of $1.2 million in general and administrative expenses associated with vacating the Richmond, Virginia facility. In December 2014, we entered into an agreement to sublet this space for the remainder of the lease term. We expect to collect proceeds from the sublease in the amount of $0.4 million over the remaining term of the lease.

As of March 31, 2015, future payments under our long-term debt agreements, the capital leases and minimum future payments under non-cancellable operating leases are as follows:

	As of March 31, 2015 Payments Due By Period				
	Total	**Less than 1 year**	**1 - 3 Years**	**4 - 5 Years**	**After 5 Years**
			(In thousands)		
Debt obligations					
Debt maturities	$ 25,000	$ 25,000	$	$	$
Contractual interest	2,356	2,356			

Capital lease obligations					
Debt maturities					
Contractual interest					
Operating leases	4,365	1,176	1,896	1,293	
Purchase obligations					
Total contractual obligations	$ 31,721	$ 28,532	$ 1,896	$ 1,293	$

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

We currently have a licensing agreement with PARI for the use of the optimized eFlow Nebulizer System for delivery of ARIKAYCE in treating patients with NTM infections, CF and bronchiectasis. We have rights to several US and foreign issued patents, and patent applications involving improvements to the optimized eFlow Nebulizer System. Under the licensing agreement, PARI is entitled to receive payments either in cash, qualified stock or a combination of both, at PARI s discretion, based on

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achievement of certain milestone events including phase 3 trial initiation (which occurred in 2012), first acceptance of MAA submission (or equivalent) in the US of ARIKAYCE and the device, first receipt of marketing approval in the US for ARIKAYCE and the device, and first receipt of marketing approval in a major EU country for ARIKAYCE and the device. In addition, PARI is entitled to receive royalty payments on commercial sales of ARIKAYCE pursuant to the licensing agreement. In July 2014, we entered into a Commercialization Agreement (the PARI Agreement) with PARI for the manufacture and supply of eFlow nebulizer systems and related accessories (the Device) as optimized for use with our proprietary liposomal amikacin for inhalation. The PARI Agreement has an initial term of fifteen years from the first commercial sale of the Device (the Initial Term). The term of the PARI Agreement may be extended by us for an additional five years by providing written notice to PARI at the least one year prior to the expiration of the Initial Term.

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

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

In February 2014, we entered into a contract manufacturing agreement with Therapure for the manufacture of ARIKAYCE at the larger scales necessary to support commercialization. Pursuant to the agreement, we are collaborating with Therapure to construct a production area for the manufacture of ARIKAYCE in Therapure s existing manufacturing facility in Mississauga, Ontario, Canada. We expect to pay Therapure approximately $12 million for the build out of the construction area and related manufacturing costs, of which approximately $8 million has been paid as of March 31, 2015. Therapure will manufacture ARIKAYCE for us on a non-exclusive basis. The agreement has an initial term of five years from the first date on which Therapure delivers ARIKAYCE to us after we obtain permits related to the manufacture of ARIKAYCE.

In December 2014, we entered into Work Order 1 (the Work Order), pursuant to a Master Agreement for Services (MSA) with SynteractHCR, Inc. (Synteract), dated as of August 27, 2014, as amended on December 23, 2014, pursuant to which we retained Synteract to perform implementation and management services in connection with certain clinical trials pursuant to a specific protocol of pharmaceutical products under development by or under the control of the Company (each, a Study). Synteract is providing comprehensive services for Protocol INS-212, a randomized, open-label, multicenter study of liposomal amikacin for inhalation in adult patients with NTM lung infections caused by MAC complex that are refractory to treatment. Prior to the execution of the Work Order, Synteract was providing such services pursuant to a Letter of Intent, dated August 25, 2014. The Work Order covers services related to INS-212 only and any additional study or services will be subject to the negotiation and execution of an additional work order. It is anticipated that aggregate costs to us relating to this Work Order will be approximately $33 million over the period of the study. In April 2015, we entered into a work order with Synteract to perform implementation and management services for Protocol INS-312.

Future Funding Requirements

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

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

- the decisions of the FDA and EMA with respect to our applications for marketing approval of ARIKAYCE in the US and Europe; the costs of activities related to the regulatory approval process; and the timing of approvals, if received;

- the cost of putting in place the sales and marketing capabilities necessary to be prepared for a potential commercial launch of ARIKAYCE, if approved;

- the cost of filing, prosecuting and enforcing patent claims;

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- the costs of our manufacturing-related activities;

- the costs associated with commercializing ARIKAYCE if we receive marketing approval; and

- subject to receipt of marketing approval, the levels, timing and collection of revenue received from sales of approved products, if any, in the future.

In April 2015, we generated proceeds of approximately $223.0 million from the issuance of 11.5 million shares of common stock. We believe we currently have sufficient funds to meet our financial needs for 2015. However, our business strategy may require us to, or we may otherwise determine to, raise additional capital at any time through equity or debt financing(s), strategic transactions or otherwise. Such additional funding may be necessary to continue to develop our potential product candidates, to pursue the license or purchase of complementary technologies, to commercialize our product candidates or to purchase other products. If we are unable to obtain additional financing, we may be required to reduce the scope of our planned product development and commercialization or our plans to establish a sales and marketing force, any of which could harm our business, financial condition and results of operations. The source, timing and availability of any future financing will depend principally upon equity and debt market conditions, interest rates and, more specifically, our continued progress in our regulatory, development and commercial activities. We cannot assure you that such capital funding will be available on favorable terms or at all. If we are unable to obtain sufficient additional funds when required, we may be forced to delay, restrict or eliminate all or a portion of our research or development programs, dispose of assets or technology or cease operations.

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

Off-Balance Sheet Arrangements

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

CRITICAL ACCOUNTING POLICIES

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

policies discussed below are considered critical to an understanding of our consolidated financial statements because their application places the most significant demands on our judgment. Actual results could differ from our estimates. 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, 2014. 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 March 31, 2015, 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 March 31, 2015, we had $25.0 million of fixed rate borrowings that bear interest at 9.25% outstanding under a Loan and Security Agreement we entered into originally in June 2012. A hypothetical 10% change in interest rates occurring on March 31, 2015 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.

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The majority of our business is conducted in US dollars. However, we do conduct certain transactions in other currencies, including Euros or British Pounds. Historically, fluctuations in foreign currency exchange rates have not materially affected our results of operations and during the three months ended March 31, 2015 and 2014, 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 March 31, 2015. 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 March 31, 2015, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures are effective at the reasonable assurance level.

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 March 31, 2015 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

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PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

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

ITEM 1A. RISK FACTORS

Except for the historical information in this report on Form 10-Q, the matters contained in this report include forward-looking statements that involve risks and uncertainties. Our operating results and financial condition have varied in the past and may in the future vary significantly depending on a number of factors. These factors, among others, could cause actual results to differ materially from those contained in forward-looking statements made in this report and presented elsewhere by management from time to time. Such factors may have a material adverse effect upon our business, results of operations and financial condition.

You should consider carefully the risk factors, together with all of the other information included in our Annual Report on Form 10-K and 10-K/A for the year ended December 31, 2014. Each of these risk factors could adversely affect our business, results of operations and financial condition, as well as adversely affect the value of an investment in our common stock. There have been no material changes to our risk factors as previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2014, except for the following updates:

Risks Related to Our Financial Condition and Capital Requirements

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

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

Under our loan agreement with Hercules, we have borrowed $25.0 million as of December 31, 2014, bearing interest of 9.25%. The maturity date for the outstanding debt is January 1, 2016, provided, however, that if a Financing Event occurs prior to December 31, 2015, we may elect to extend such maturity date to January 1, 2018. A Financing Event means that we have (1) received unrestricted and unencumbered (other than liens or encumbrances evidenced by subordinated indebtedness) net cash proceeds in an amount equal to or greater than Ninety Million Dollars ($90 million), resulting from (a) the issuance and sale by us of our equity securities, and/or (b) subordinated indebtedness, and/or (c) upfront cash payments paid to us in conjunction with a development and/or commercial partnership(s) and/or other corporate transactions, and (2) paid Hercules a fully- earned, non-refundable fee in the amount of Two Hundred Fifty Thousand Dollars ($250,000). We completed an equity financing in April 2015 in excess of $90.0 million, which we believe qualifies as a Financing Event under our loan agreement. Our borrowings under the Loan Agreement are secured by a lien on our assets, excluding our intellectual property, and in the event of a default on the loan, the lender may have the right to seize our assets securing our obligations under the Loan Agreement. The terms and restrictions provided for in the Loan Agreement may inhibit our ability to conduct our business and to provide distributions to our stockholders. Future debt securities or other financing arrangements could contain negative covenants similar to, or even more restrictive than, the Hercules loan.

Risks Related to Regulatory Matters

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

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

Data submitted to the regulators is subject to varying interpretations that could delay, limit or prevent regulatory agency approval. We may also encounter delays or rejections based on changes in regulatory agency policies during the period in which we develop a product and the period required for review of any application for regulatory agency approval of a particular product. For example, FDA has designated ARIKAYCE for Fast Track, Breakthrough Therapy and QIDP status, all programs intended to expedite or simplify 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.

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

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

To market our products outside of the U.S. and Europe, we and any potential third parties must comply with numerous and varying regulatory requirements of other countries. The approval procedures vary among countries and can involve additional product testing and administrative review periods. The time required to obtain approval in these other territories might differ from that required to obtain FDA or EMA approval. The regulatory approval process in these other territories includes at least all of the risks associated with obtaining FDA and EMA approval detailed above.

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

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

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 March 31, 2015.

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ITEM 3. **DEFAULTS UPON SENIOR SECURITIES**

None.

ITEM 4. **MINE SAFETY DISCLOSURES**

Not applicable.

ITEM 5. **OTHER INFORMATION**

None.

ITEM 6. **EXHIBITS**

A list of exhibits filed herewith is included on the Exhibit Index, which immediately precedes such exhibits and is incorporated herein by reference.

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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: May 7, 2015 By /s/ Andrew T. Drechsler
Andrew T. Drechsler
Chief Financial Officer

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EXHIBIT INDEX

10.1	Employment Agreement, effective as of February 18, 2014, between Insmed Incorporated and Peggy Berry.
10.2	Employment Agreement, effective as of January 2, 2013, between Insmed Incorporated and S. Nicole Schaeffer.
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 Andrew T. Drechsler, Chief Financial 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 Andrew T. Drechsler, Chief Financial 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.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document