INSMED INC
Form 10-Q
May 08, 2014
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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, 2014

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.)
9 Deer Park Drive, Suite C **Monmouth Junction, New Jersey**	**08852**
(Address of principal executive offices)	(Zip Code)

(732) 997-4600

(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 o Accelerated filer x 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, 2014, there were 39,272,501 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, 2014

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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. ARIKACE® and IPLEX® are registered trademarks of Insmed Incorporated. ARIKAYCETM and INSMEDTM 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, 2014 (unaudited)	As of December 31, 2013
Assets		
Current assets:		
Cash and cash equivalents	$ 101,251	$ 113,894
Prepaid expenses and other current assets	4,958	2,269
Total current assets	106,209	116,163
In-process research and development	58,200	58,200
Other assets	234	323
Fixed assets, net	1,977	1,812
Total assets	$ 166,620	$ 176,498
Liabilities and shareholders equity		
Current liabilities:		
Accounts payable	$ 9,818	$ 5,929
Accrued expenses	3,143	3,905
Accrued compensation	1,371	2,839
Accrued lease expense, current	310	307
Deferred rent	121	129
Capital lease obligations, current	48	64
Current portion of long term debt	5,187	3,283
Total current liabilities	19,998	16,456
Accrued lease expense, long-term	315	380
Debt, long-term	14,569	16,338
Total liabilities	34,882	33,174
Shareholders equity:		
Common stock, $0.01 par value; 500,000,000 authorized shares, 39,268,885 and 39,137,679 issued and outstanding shares at March 31, 2014 and December 31, 2013, respectively.	393	391
Additional paid-in capital	537,264	534,554
Accumulated deficit	(405,919)	(391,621)
Total shareholders equity	131,738	143,324
Total liabilities and shareholders equity	$ 166,620	$ 176,498

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,	
	2014	**2013**
Revenues	$	$
Operating expenses:		
Research and development	11,351	10,334
General and administrative	6,728	3,975
Total operating expenses	18,079	14,309
Operating loss	(18,079)	(14,309)
Investment income	17	51
Interest expense	(606)	(643)
Other, net	(19)	2
Loss before income taxes	(18,687)	(14,899)
(Benefit) from income taxes	(4,389)	(1,221)
Net loss and comprehensive loss	$ (14,298)	$ (13,678)
Basic and diluted net loss per share	$ (0.36)	$ (0.43)
Weighted average basic and diluted common shares outstanding	39,240	31,554

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,	
	2014	**2013**
Operating activities		
Net loss	$ (14,298)	$ (13,678)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	167	148
Stock based compensation expense	2,358	954
Gain on sale of asset, net		(2)
Amortization of debt discount and debt issuance costs	102	118
Accrual of the end of term charge on the debt	33	49
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(2,600)	(797)
Accounts payable	3,889	1,124
Accrued expenses and deferred rent	(770)	1,787
Accrued lease expenses	(62)	(64)
Accrued compensation	(1,468)	(848)
Net cash used in operating activities	(12,649)	(11,209)
Investing activities		
Purchase of fixed assets	(331)	(163)
Proceeds from sale of asset		2
Net cash used in investing activities	(331)	(161)
Financing activities		
Payments on capital lease obligations	(16)	(29)
Proceeds from exercise of stock options	353	51
Net cash provided by financing activities	337	22
Decrease in cash and cash equivalents	(12,643)	(11,348)
Cash and cash equivalents at beginning of period	113,894	90,782
Cash and cash equivalents at end of period	$ 101,251	$ 79,434
Supplemental disclosures of cash flow information:		
Cash paid for interest	$ 463	$ 476
Cash received for taxes	$ 4,389	$ 1,221

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 focused on developing and commercializing inhaled therapies for patients battling serious lung diseases that are often life threatening. The Company s lead product candidate, ARIKAYCETM, or liposomal amikacin for inhalation, is an inhaled antibiotic treatment that delivers a proven and potent anti-infective directly to the site of serious lung infections. 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 Merger). The Company s continuing operations are based on the technology and products historically developed by Transave. The Company s principal executive offices are located in Monmouth Junction, New Jersey.

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, 2013.

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, and Celtrix Pharmaceuticals, Incorporated. 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, 2013:

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.

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- Level 3 Inputs reflect management s best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

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

The following table presents assets and liabilities measured at fair value as of March 31, 2014 and December 31, 2013 (in thousands):

		Total	Fair Value Measurements at Reporting Date Using Quoted Prices in Active Markets for Identical Assets (Level 1)	Quoted Prices in Inactive Markets for Identical Assets (Level 2)	Significant Unobservable Inputs (Level 3)
As of March 31, 2014:					
Assets:					
Cash and cash equivalents	$	101,251	$ 101,251	$	$
	$	101,251	$ 101,251	$	$
As of December 31, 2013:					
Assets:					
Cash and cash equivalents	$	113,894	$ 113,894	$	$
	$	113,894	$ 113,894	$	$

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, 2014 and March 31, 2013.

As of March 31, 2014 and December 31, 2013, 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

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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, 2014 and 2013:

	2014	2013
	(In thousands, except per share amounts)	
Numerator:		
Net loss:	$ (14,298)	$ (13,678)
Denominator:		
Weighted average common shares used in calculation of basic net loss per share:	39,240	31,554
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	39,240	31,554
Net loss per share:		
Basic and Diluted	$ (0.36)	$ (0.43)

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

	2014	2013
Warrants to purchase common stock		330
Stock options to purchase common stock	4,230	2,348
Restricted stock and restricted stock units	18	200

3. Identifiable Intangible Assets and Goodwill

The Company believes there are no indicators of impairment relating to its in-process research and development intangible assets as of March 31, 2014.

4. Accrued Expenses

Accrued expenses consist of the following:

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	As of March 31, 2014	As of December 31, 2013
	(in thousands)	
Accrued clinical trial expenses	$ 1,444	$ 2,484
Accrued technical operation expenses	751	1,220
Accrued professional fees	764	24
Accrued interest payable	159	159
Other accrued expenses	25	18
	$ 3,143	$ 3,905

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 allowed the Company to borrow up $20.0 million in $10.0 million increments (Loan Agreement). The Company borrowed the first and second $10.0 million increments by signing two Secured Promissory Notes (Note A and Note B and collectively, the Notes) on June 29, 2012 and December 27, 2012, respectively. Notes A and B bear interest at 9.25%. Note A was originally scheduled to be repaid over a 42-month period with the first twelve monthly payments representing interest only followed by thirty monthly equal payments of principal and interest. Note B was originally scheduled to be repaid over a 36-month period with the first six monthly payments representing interest only followed by thirty monthly equal payments of principal and interest. The Loan Agreement provided that in certain circumstances the Company could delay the first principal payment by five months. In July 2013, subsequent to the completion of certain ARIKAYCE-related development milestones, the Company elected to extend the interest only period under the Notes from July 31, 2013 to December 31, 2013 and delay the first monthly principal repayments for Notes A and B from August 1, 2013 to January 1, 2014. On November 25, 2013, the Company and Hercules entered into an amendment (the Amendment) of the Loan Agreement. Pursuant to the Amendment, the interest-only period has been extended through June 30, 2014 and the first monthly principal payment is scheduled for July 1, 2014. The Amendment also allows the Company to further extend the interest-only period through December 31, 2014 and delay the first payment of principal until January 1, 2015, so long as the Company pays a $100,000 fee and obtains positive data from its phase 2 clinical trial of ARIKAYCE in patients who have lung infections caused by nontuberculous mycobacteria (NTM). The election and amendment did not change the maturity date for Notes A and B, which is January 1, 2016.

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

The Loan Agreement also contains representations and warranties by the Company and the lender and indemnification provisions in favor of the lender and customary covenants (including limitations on other indebtedness, liens, acquisitions, investments and dividends, but no financial covenants), and events of default (including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of the lender s security interest or in the collateral, and events relating to bankruptcy or insolvency). Upon the occurrence of an event of default, a default interest rate of an additional 5% may be applied to the outstanding loan balances, and the lender may terminate its lending commitment, declare all outstanding

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obligations immediately due and payable, and take such other actions as set forth in the Loan Agreement. In addition, pursuant to the Loan Agreement, the lender has the right to participate, in an amount of up to $1.0 million, in certain future private equity financing(s) by the Company.

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

The following table presents the components of the Company s debt balance as of March 31, 2014:

		March 31, 2014 (in thousands)
Debt:		
Notes payable	$	20,000
Accretion of end of term charge		237
Issuance fees paid to lender		(179)
Discount from warrant		(302)
Current portion of long-term debt		(5,187)
Long-term debt	$	14,569

As of March 31, 2014, future principal repayments of the two Notes for the period April 1, 2014 to December 31, 2014 and in each of the years ending December 31, 2015 and 2016 were as follows (in thousands):

Year Ending in December 31:		
2014	$	3,626
2015		7,785
2016		8,589
	$	20,000

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

6. Stockholders Equity

Common Stock As of March 31, 2014, the Company had 500,000,000 shares of common stock authorized with a par value of $0.01 and 39,268,885 shares of common stock issued and outstanding. Of the shares outstanding as of March 31, 2014, 1,765,271 shares represent holdback shares held by the Company as security for potential indemnification payments, as described in the Agreement and Plan of Merger

with Transave (the Merger Agreement), filed as Exhibit 2.1 to the Company s Annual Report on Form 10-K for the year ended December 31, 2012 (see Note 10, Commitments and Contingencies, Legal Proceedings, Pilkiewicz v. Transave LLC for additional information regarding these holdback shares). In addition, as of March 31, 2014, the Company had reserved 4,229,646 shares of common stock for issuance upon the exercise of outstanding common stock options and 18,270 for issuance upon the vesting of restricted stock units.

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

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

Warrant - In conjunction with entering into the Loan Agreement (See Note 5 Debt), the Company granted a warrant to the lender to purchase 329,932 shares of the Company s common stock at an exercise price of $2.94 per share. The fair value of the warrant of $0.8 million was calculated using the Black-Scholes warrant-pricing methodology at the date of issuance and was recorded as equity and as a discount to the debt and is being amortized to interest expense over the term of the related debt using the effective interest method. On April 30, 2013, the lender exercised the warrant in full via the net issuance method specified in the warrant agreement. In accordance with such provisions, the Company issued and delivered 223,431 shares of common shares to the lender on May 1, 2013. As a result of the exercise, the warrant is no longer outstanding and there are no additional shares issuable under this instrument.

7. Stock-Based Compensation

During 2013, the Company had three equity compensation plans: 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 Amended and Restated 2000 Stock Incentive Plan, as amended (the 2000 Stock Incentive Plan) and the Amended and Restated 2000 Employee Stock Purchase Plan (the Stock Purchase Plan). Both the 2000 Stock Incentive Plan and the Stock Purchase Plan were adopted by the Company s Board of Directors and approved by the Company s shareholders in 2000. Upon the approval of the 2013 Incentive Plan, no additional awards were issued under the 2000 Stock Incentive Plan and the shares remaining for future grant under the 2000 Stock Incentive Plan were transferred to the 2013 Incentive Plan. The 2013 Incentive Plan is administered by the Compensation Committee and the Board of Directors of the Company. On October 31, 2013, the Company s Board of Directors terminated the Stock Purchase Plan.

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 shares and other stock awards, as well as the payment of incentive bonuses to all employees and non-employee directors. The 2013 Incentive Plan provides for a single aggregate per person annual sub-limit of 1,500,000 stock options, performance shares (including restricted stock units, or RSUs) and shares of restricted stock. The 2013 Incentive Plan provides for the issuance of a maximum of 3,053,833 shares of common stock. Shares subject to outstanding awards under the 2000 Stock Incentive Plan that are cancelled, expired, forfeited or otherwise not issued will also be added to the number of shares available under the 2013 Incentive Plan. As of March 31, 2014, 1,162,113 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.

Under the terms of the 2000 Stock Incentive Plan, the Company was 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), restricted stock, RSU s, performance shares, and other stock awards to all employees and non-employee directors. On March 15, 2013, the Company s Board of Directors amended the 2000 Stock Incentive Plan to provide for a single aggregate per person annual sub-limit for the issuance of a maximum of 1,500,000 stock options, performance shares (including RSUs) and shares of restricted stock. The 2000 Stock Incentive Plan ceased to be available for additional grants once the Company s shareholders approved the 2013 Incentive Plan on May 23, 2013.

During the first quarter of 2013, the Company completed a review of equity compensation awards granted under its 2000 Stock Incentive Plan and determined that it had inadvertently exceeded the annual per-person sub-limits involving certain awards previously made to certain of its current and past officers and directors (the excess awards). The aggregate amount of common stock represented by these excess awards, which

consisted of RSUs

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and stock options, was approximately 1.4 million shares. These awards were deemed to be granted outside of the 2000 Stock Incentive Plan and as such the Company applied liability accounting to these awards. On May 23, 2013 (the date of the Company s 2013 Annual Meeting of Stockholders), the Company s shareholders approved the grants associated with the excess awards, which as of that date, allowed the excess awards to be deemed granted under the 2000 Stock Incentive Plan. As a result, the excess awards were remeasured at fair value on May 23, 2013 and the liability was reclassified to additional paid-in capital. The unrecognized fair value calculated for the excess awards as of May 23, 2013 is recognized as compensation expense ratably over the remaining requisite service period for each award.

Stock Options - The Company calculates the fair value of stock options granted using the Black-Scholes valuation model.

The following table summarizes the Company s grant date fair value and assumptions used in determining the fair value of stock options granted under and outside the 2013 Incentive Plan and the 2000 Stock Incentive Plan:

	Three Months Ended March 31,	
	2014	**2013**
Volatility	83.6% - 85.5%	93.9% - 96.0%
Risk-free interest rate	1.46% - 1.76%	0.76% - 0.85%
Dividend yield	0.0%	0.0%
Expected option term (in years)	6.25	6.25
Weighted-average fair value of stock options granted	$14.35	$5.30

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 US 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.

The following table summarizes the Company s stock option activity for the three months ended March 31, 2014:

	Number of Shares	**Weighted Average Exercise Price**	**Weighted Average Remaining Contractual Life in Years**	**Aggregate Intrinsic Value (in thousands)**
Options outstanding at December 31, 2013	3,632,996	$ 7.94		
Granted	649,050	19.78		
Exercised	(52,400)	6.73		
Forfeited or expired				
Options outstanding at March 31, 2014	4,229,646	$ 9.77	8.97	$ 39,808
Vested and expected to vest at March 31, 2014	3,968,337	$ 9.65	8.96	$ 37,812
Exercisable at March 31, 2014	617,662	$ 4.23	8.18	$ 9,148

The total intrinsic value of stock options exercised during the three months ended March 31, 2014 and 2013 was $0.6 million, and $0.1 million, respectively.

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As of March 31, 2014, there was $30.0 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. The following table summarizes the range of exercise prices and the number of stock options outstanding and exercisable:

$ 3.03	$ 3.29	276,787	7.75	$ 3.04	133,502	$ 3.04
$ 3.40	$ 3.40	708,314	8.45	$ 3.40	265,619	$ 3.40
$ 3.48	$ 6.70	434,845	8.37	$ 5.59	149,355	$ 5.46
$ 6.90	$ 6.96	474,700	8.92	$ 6.91	62,436	$ 6.92
$ 7.44	$ 10.35	436,950	8.93	$ 7.75	6,750	$ 8.11
$ 11.14	$ 11.46	257,000	9.34	$ 11.22		
$ 12.44	$ 12.44	551,300	9.15	$ 12.44		
$ 12.78	$ 16.19	450,700	9.57	$ 14.57		
$ 16.54	$ 20.49	624,050	9.83	$ 19.81		
$ 21.54	$ 21.54	15,000	9.81	$ 21.54		

Restricted Stock and Restricted Stock Units The Company may grant Restricted Stock (RS) and RSUs to eligible employees, including its executives, and non-employee directors. Each RS and RSU represents a right to receive one share of the Company s common stock upon the completion of a specific period of continued service or achievement of a certain milestone. RS and RSU awards granted under the 2013 Incentive Plan and 2000 Stock Incentive Plan are generally valued at the market price of the Company s common stock on the date of grant. RSUs granted in excess of certain plan sub-limits were considered to be granted outside the 2000 Stock Incentive Plan and were classified as a liability and remeasured at fair value at the end of each reporting period and changes in fair value are included in compensation expense in the Consolidated Statements of Comprehensive Loss (see additional disclosures related to RSUs granted outside the 2000 Stock Incentive Plan at the end of this note). 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 awards activity during the three months ended March 31, 2014:

	Number of RSU s	Weighted Average Grant Price
Outstanding at December 31, 2013	92,641	$ 6.27
Granted	17,568	20.49
Released	(91,939)	6.21
Outstanding at March 31, 2014	18,270	$ 20.25
Expected to vest	18,270	$ 20.25

Awards Granted Outside of the 2000 Stock Incentive Plan As described above, during the first quarter of 2013, the Company completed a review of equity compensation awards granted under its 2000 Stock Incentive Plan and determined that it had inadvertently exceeded the annual per-person sub-limits involving certain awards previously made to certain of its current and past officers and directors. The aggregate amount of common stock represented by these excess awards, which consisted of RSUs and stock options, was approximately 1.4 million shares. These awards were deemed to be granted outside of the 2000 Stock Incentive Plan and as such the Company applied liability accounting to these awards. On May 23, 2013 (the date of the Company s 2013 Annual Meeting of

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Stockholders), the Company s shareholders approved the grants associated with the excess awards, which as of that date, allowed the excess awards to be deemed granted under the 2000 Stock Incentive Plan. As a result, the excess awards were remeasured at fair value on May 23, 2013 and the liability was reclassified to additional paid-in capital. The unrecognized fair value calculated for the excess awards as of May 23, 2013 will be recognized as compensation expense ratably over the remaining requisite service period for each award.

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, 2014 and 2013:

	2014	2013
	(in millions)	
Research and development expenses	$ 0.9	$ 0.2
General and administrative expenses	1.5	0.8
Total	$ 2.4	$ 1.0

8. Income Taxes

The benefit for income taxes was $4.4 million and $1.2 million for the three months ended March 31, 2014 and 2013, respectively. The benefit for income taxes recorded for the three months ended March 31, 2014 and 2013 solely reflect 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 and $1.2 million, respectively and net of commissions. The Program allows qualified technology and biotechnology businesses in New Jersey to sell unused amounts of NOLs and defined research and development tax credits for cash.

The Company is subject to US federal and state income taxes. The Company has never been audited and the statute of limitations for tax audit is generally open for the years 2010 and later. The Company has incurred net operating losses since inception, except in 2009. Such loss carryforwards would be subject to audit in any tax year in which those losses are utilized, notwithstanding the year of origin. The Company s policy is to recognize interest accrued related to unrecognized tax benefits and penalties in income tax expense. The Company has recorded no such expense. As of March 31, 2014 and December 31, 2013, 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. Due to the Company s history of operating losses, the Company recorded a full valuation allowance on its net deferred tax assets as it is more likely than not that such tax benefits will not be realized.

At December 31, 2013, the Company had federal net operating loss carryforwards for income tax purposes of approximately $398.7 million available to offset future taxable income, if any. The NOL carryovers and general business tax credits expire in various years beginning in 2018.

Utilization of the Company s NOL and general business tax credit carryforwards generated in prior years through September 2012 (the September 2012 and prior NOLs) are likely subject to substantial limitations under Section 382 of the Internal Revenue Code (Section 382) due to ownership changes that occurred at various points during years prior to 2012 and during September 2012. 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

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raised capital through the issuance of common stock on several occasions which, combined with the purchasing shareholders subsequent disposition of those shares, likely resulted in multiple changes in ownership, as defined by Section 382 since the Company s formation in 1999. The substantial limitations on the use of the September 2012 and prior NOLs are likely to result in expiration of a substantial portion of these NOL or general business tax credit carryforwards before utilization which would substantially reduce the Company s gross deferred tax assets. The Company plans to complete a Section 382 analysis regarding the limitation of its NOL and general business tax credit carryforwards and intends to disclose the results of this analysis when it is completed.

9. Contract Manufacturing Agreement

Therapure Biopharma Inc. In February 2014, the Company entered into a Contract Manufacturing Agreement (the Agreement) with Therapure Biopharma Inc. (Therapure) for the manufacture of the Company s product ARIKAYCE. Pursuant to the Agreement, the Company and Therapure will collaborate to construct a production and quality control area for the manufacture and testing of ARIKAYCE in Therapure s existing manufacturing facility in Mississauga, Ontario, Canada. Therapure will manufacture ARIKAYCE for the Company on a non-exclusive basis. The Agreement has an initial term of five years from the first date on which Therapure delivers ARIKAYCE to Insmed after Insmed obtains permits related to the manufacture of ARIKAYCE, and will renew automatically for successive periods of two years each, unless terminated by either party by providing the required two years prior written notice to the other party. Notwithstanding the foregoing, the parties have rights and obligations under the Agreement prior to the commencement of the initial term. The Agreement allows for termination by either party upon the occurrence of certain events, including, (i) the material breach by the other party of any provision of the Agreement or the quality agreement expected to be entered into between the parties, or (ii) the default or bankruptcy of the other party. In addition, the Company may terminate the Agreement for any reason upon no fewer than one hundred eighty days advance notice. Costs incurred under this agreement will be recorded as a component of research and development expense until such time as the Company receives United States Food and Drug Administration approval for ARIKAYCE.

10. Commitments and Contingencies

Commitments

The Company has two operating leases for office and laboratory space located in Monmouth Junction, New Jersey through December 31, 2014. Future minimum rental payments under these two leases total approximately $0.5 million. The Company also has an operating lease for office and laboratory space located in Bridgewater, New Jersey that terminates in November 2019. Future minimum rental payments under this lease as of March 31, 2014 were $2.4 million. The Company also leases office space in Richmond, Virginia, where the Company s corporate headquarters were previously located, through October 2016. Future minimum rental payments under this lease as of March 31, 2014 total approximately $1.3 million.

Rent expense charged to operations was $0.3 million and $0.2 million for the three months ended March 31, 2014 and 2013, respectively. Future minimum rental payments required under the Company s operating leases for the period from April 1, 2014 to December 31, 2014 and for each of the next five years are as follows (in thousands):

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2014 (remaining)	$	938
2015		945
2016		885
2017		474
2018		488
2019		460
	$	4,190

Legal Proceedings

Pilkiewicz v. Transave LLC

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

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

Under the terms of the Merger Agreement, certain of the former stockholders of Transave (the Transave Stockholders) are obligated to indemnify the Company for certain liabilities in connection with the appraisal action. The Company notified the Transave Stockholders in May 2012 that the Company is seeking indemnification in accordance with the Merger Agreement and that it will continue to retain the aggregate amount of the holdback shares totaling 1,765,271 shares, as security for any indemnification payments due under the Merger Agreement. Discovery was completed and a trial was scheduled to begin in April 2014. Prior to commencement of the trial, the parties agreed to settle the matter and are in the process of negotiating a settlement agreement. The Company expects to be indemnified in full for the settlement and related costs incurred in defending the appraisal action.

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

11. Retirement Plan

The Company has a 401(k) defined contribution plan for the benefit for all employees and permits voluntary contributions by employees subject to IRS-imposed limitations. There were no employer contributions in the three months ended March 31, 2014 and 2013.

12. Subsequent Events

On April 2, 2014, the Company announced that Dr. Renu Gupta, a Named Executive Officer, will transition to a new role as Special Advisor to the Chief Executive Officer, effective as of April 21, 2014. She will serve in this position until her departure from the Company later this year. The Company expects to incur certain one-time expenses related to her Transition & Separation Agreement beginning in the second quarter of 2014.

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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 raise additional capital; our ability to complete development of, receive regulatory approval for, and successfully commercialize ARIKAYCETM; 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 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, 2013 filed with the Securities and Exchange Commission (SEC) on March 6, 2014. 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.

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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, 2013.

OVERVIEW

Insmed is a biopharmaceutical company focused on developing and commercializing inhaled therapies for patients battling serious lung diseases that are often life threatening. Our lead product candidate, ARIKAYCE™, or liposomal amikacin for inhalation (LAI), is an inhaled antibiotic treatment that delivers a proven and potent anti-infective directly to the site of serious lung infections.

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 have lung infections caused by nontuberculous mycobacteria (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 although there was a positive trend (p=0.148) in favor of ARIKAYCE. However, ARIKAYCE did achieve statistical significance with regard to the clinically relevant key secondary endpoint of culture conversion, with 11 out of 44 patients treated with ARIKAYCE (added to standard of care treatment) demonstrating negative cultures by 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). Data analyses for certain additional secondary, tertiary and exploratory endpoints are ongoing. We plan to present additional data at the American Thoracic Society meeting in May 2014. We also applied for Breakthrough Therapy Designation for ARIKAYCE in the US based upon the culture conversion results in our phase 2 clinical trial. ARIKAYCE has already received Orphan Drug, Qualified Infectious Disease Product (QIDP) and Fast Track designations from the US Food and Drug Administration (FDA) for the treatment of NTM lung infections and recently received Orphan Drug Designation from the European Medicines Agency (EMA).

In 2013, we concluded a phase 3 clinical trial in Europe and Canada of ARIKAYCE in cystic fibrosis (CF) patients who have lung infections caused by *Pseudomonas aeruginosa* (*Pseudomonas*). In this study, once-daily ARIKAYCE achieved its primary endpoint of non-inferiority when compared to twice-daily TOBI® (tobramycin inhaled solution) for relative change in forced expiratory volume in one second from baseline to the end of the study.

The CF and NTM target indications address orphan patient populations. Our strategy includes plans to continue to develop ARIKAYCE to broaden the NTM indication and for additional indications beyond *Pseudomonas* in CF and NTM. We also plan to develop, acquire, in-license or co-promote other products that address orphan or rare diseases in the fields of pulmonology and infectious disease. Our current primary development focus is to obtain regulatory approval for ARIKAYCE in these two initial indications and to prepare for commercialization in the US, Europe, Canada and Japan. We anticipate that if approved, ARIKAYCE would be the first once-a-day inhaled antibiotic treatment option available for these CF and NTM indications. The following table summarizes the current status of ARIKAYCE development.

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Product Candidate/Target Indications	Status	Next Expected Milestones
ARIKAYCE Non-tuberculous mycobacteria (NTM) lung infections	• 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 did achieve statistical significance with regard to the clinically relevant key secondary endpoint of culture conversion. • Granted orphan drug designation in Europe and the US. • Granted QIDP designation, which includes Priority Review, by the FDA in June 2013. • Granted Fast Track designation by the FDA in June 2013 which permits a rolling submission of an NDA. • Applied for Breakthrough Therapy Designation for ARIKAYCE in the US in April 2014 based upon the culture conversion results in the phase 2 clinical trial.	• We expect to commence an additional study in the US and/or Europe in the second half of 2014. • We expect to have dialogue with the FDA and the EMA in the next several months to discuss the regulatory pathway. • If approved, we expect ARIKAYCE would be the first approved inhaled antibiotic treatment for NTM lung infections. • We are developing plans to commercialize ARIKAYCE, if approved, initially in the US, in certain countries in Europe, and Canada and eventually Japan.
ARIKAYCE *Pseudomonas aeruginosa* lung infections in CF patients	• Reported top-line results from our phase 3 clinical trial for registration in Europe and Canada in July 2013, in which once-daily ARIKAYCE achieved its primary endpoint of non-inferiority when compared to twice-daily tobramycin inhaled solution. • Conducting a two-year, open-label safety study in patients that completed our phase 3 clinical trial in Europe and Canada. We expect to complete this study in mid-2015. • Reported top-line results from the first group of patients that completed the first year of the two-year open label extension study. • Granted orphan drug designation in Europe and the US.	• We expect to submit regulatory filings with the EMA and Health Canada (the government agency that provides regulatory and marketing approval for drugs and therapeutic products in Canada) in the second half of 2014. If the EMA allows a filing that includes both the CF and NTM indications we will most likely submit our filing in the second half of 2014. • We are developing plans to commercialize ARIKAYCE, if approved, in certain countries in Europe and in Canada where we expect it would be the only once-a-day treatment for *Pseudomonas* lung infections in CF patients. • We expect to reevaluate our plans regarding a US phase 3 clinical trial in CF patients with *Pseudomonas* lung infection after we receive the final results from the ongoing phase 2 clinical trial in NTM patients in the US.
ARIKAYCE *Pseudomonas aeruginosa* and other susceptible organisms causing lung infections in non-CF bronchiectasis patients	• Completed phase 2 study in the US. • Granted orphan drug designation in the US.	• We do not intend to initiate further clinical studies with respect to a non-CF bronchiectasis indication until we have completed additional clinical studies for CF patients with *Pseudomonas* lung infections and for patients with NTM lung

	infections. Following those studies, we will evaluate whether to develop ARIKAYCE further for non-CF bronchiectasis.

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For FDA marketing application and review purposes, ARIKAYCE is considered a new molecular entity (NME) primarily due to its proprietary liposomal technology. The FDA has indicated that it considers ARIKAYCE a NME for application and review purposes even though the agency has previously approved drugs with the active ingredient, amikacin sulfate. FDA characterizes some drugs as NMEs for administrative purposes, even if they contain an active moiety (the molecule or ion responsible for the action of the drug substance) that is closely related to active moieties in products that have previously been approved by FDA. Amikacin sulfate is an FDA-approved antibiotic with proven efficacy in the treatment of a broad range of gram-negative infections, including *Pseudomonas* and NTM. ARIKAYCE is in the aminoglycoside class of antibiotics.

If approved for NTM patients, we believe ARIKAYCE would be the first and only approved inhaled antibiotic for the treatment of NTM lung infections. If approved for CF patients with *Pseudomonas* lung infections, we believe ARIKAYCE would be the first inhaled antibiotic to be approved for once-daily administration in this indication. ARIKAYCE has been granted the following orphan drug designations:

- US: NTM lung infections, *Pseudomonas* lung infections in CF patients, and lung infections in non-CF bronchiectasis patients; and
- European Union (EU): NTM lung infections and *Pseudomonas* lung infections in CF patients.

Corporate History

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

Our Strategy

Our strategy is to focus on the development and commercialization of innovative inhaled 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 generating additional clinical data from studies showing the effects of ARIKAYCE to treat NTM lung infections and *Pseudomonas* lung infections in CF patients necessary for new drug applications in Europe, Canada, Japan and the US;
- Actively pursue new drug filings to secure approval for ARIKAYCE to treat NTM lung infections in the US, Europe, Canada and Japan;
- Actively pursue new drug filings to secure approval for ARIKAYCE to treat *Pseudomonas* lung infections in CF patients 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 including Korea, Taiwan and China;

- Prepare for commercial launch in *Pseudomonas* 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 or to enable pursuit of a new indication.

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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 plan to submit regulatory filings in Europe and Canada for the CF indication in the second half of 2014 and, if the EMA allows, the filing will include both the CF and NTM indications. In the first quarter of 2014 we completed the double blind phase of our US and Canadian phase 2 clinical study of ARIKAYCE in patients with recalcitrant NTM lung infections. We expect to commence an additional study in the second half of 2014 for patients with NTM lung infections. We plan to scale up manufacturing, we are identifying 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. We also intend to continue to work closely 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 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 we have exclusive access to this technology, which is specifically developed for the delivery of our liposomal encapsulation of amikacin, through our licensing agreement with PARI. Our proprietary liposomal technology and the nebulizer are designed specifically for delivery of pharmaceuticals to the lung and provides 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 to be approximately $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 for approximately 13 minutes via inhalation using the eFlow® Nebulizer System, which has been optimized specifically for ARIKAYCE by PARI. We believe that this nebulizer system will reduce treatment time or dosing frequency, as compared with the currently marketed inhaled antibiotics, which require dosing two to three times daily with treatment times ranging from approximately 10 to 40 minutes per day. By easing the patient s treatment burden we believe that 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 benefit.

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

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as compared to existing products. In the future we may conduct head-to-head comparative studies that would be necessary to make comparative statements against other products.

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

Current Treatment Options and Limitations

We believe there currently is no drug approved in Europe or the US 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 standard treatment regimen for some NTM patients. It is delivered most commonly by intravenous administration and, far less often, by inhalation. Because the drug is delivered for months at a time, resulting in high systemic (blood) levels of the drug, there can be considerable toxicity, including ototoxicity and nephrotoxicity, associated with intravenous treatment. There are very 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.

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

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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 twenty-eight 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.

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.

ARIKAYCE for NTM Lung Infections: Potential Advantages and Distinguishing Features

If approved, we believe ARIKAYCE would be the first and only approved treatment 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.

Preclinical Activity

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

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.

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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 for approximately 13 minutes per day for a period of 84 days for this indication. We believe that an effective inhaled treatment that improves the outcomes for an NTM patient would represent a significant benefit in the patient s quality of life.

Current Clinical Program

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 although there was a positive trend in favor of ARIKAYCE. However, ARIKAYCE did achieve statistical significance with regard to the clinically relevant key secondary endpoint of culture conversion, with 11 out of 44 patients treated with ARIKAYCE (added to standard of care treatment) demonstrating negative cultures by day 84 of the study as compared to 3 out of 45 patients treated with placebo (added to standard of care treatment). Data analyses for certain additional secondary, tertiary and exploratory endpoints are ongoing. We plan to present additional data at the American Thoracic Society meeting in May 2014 and we applied for Breakthrough Therapy Designation for ARIKAYCE in the United States based upon the culture conversion results in our phase 2 clinical trial. Additionally, we have initiated a scintigraphy sub-study to examine drug deposition and distribution of ARIKAYCE in the lung.

There was a pre-specified stratification of patients with MAC versus *M. abscessus* and patients with and without cystic fibrosis. The study also measured certain secondary, tertiary and exploratory endpoints, including but not limited to: the proportion of patients with culture conversion to negative, the time to rescue anti-mycobacterial drugs, the change from baseline in six-minute walk distance and oxygen saturation, the change from baseline in patient reported outcomes, and evaluation of safety and tolerability.

In addition to the phase 2 clinical trial outlined above, we intend to commence an additional study in the second half of 2014 with planned sites in the US and Europe.

ARIKAYCE received orphan drug status in the US and Europe for the treatment of NTM.

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 free amikacin. We believe that the safety and efficacy data obtained from the phase 3, phase 2 and open label studies of ARIKAYCE in CF and non-CF patients with chronic lung disease and pulmonary infections and the non-clinical data collected to date serve as the basis for further development of ARIKAYCE in patients with NTM lung infections.

We submitted an IND to launch a phase 3 study of ARIKAYCE in CF and non-CF patients with recalcitrant NTM lung disease. In August 2011, prior to starting the NTM study, we announced that the FDA placed

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a clinical hold on our phase 3 trial for ARIKAYCE in patients with recalcitrant NTM lung infections. 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 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 immediately have a 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. In 2013, we commenced preparations for the potential commercialization of ARIKAYCE, including hiring Matt Pauls, our Chief Commercial Officer. We plan to fill several other new positions to support our future sales and marketing efforts. We may also seek to out-license ARIKAYCE outside of Europe, Canada and the US.

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 about 37 years (Cystic Fibrosis Foundation Patient Registry, 2011). Median predicted age of survival is calculated using life table analysis (as calculated by actuaries) given the ages of the patients in the registry and the distribution of deaths. Using this calculation, half of the people in the patient registry are expected to live beyond the median predicted survival age, and half are expected to live less than the median predicted survival age.

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

bacteria, reduce inflammation and preserve lung function for as long as possible. The rate of infection with *Pseudomonas* in CF patients increases with age. It is estimated that 70% of adult CF patients have chronic infection due to *Pseudomonas* (CFF Patient Registry, 2011). A study reported in the *Journal of Cystic Fibrosis*

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(Liou, 2010) found that deterioration in lung function of CF patients is the main cause of death and that, despite best efforts, lung function declines by 1% to 3% annually.

Current Treatment Options and Limitations

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

Antibiotics delivered via inhalation are part of the standard treatment for CF patients with *Pseudomonas* lung infections and are generally thought to be a way to deliver more active drug directly to the site of infection compared with other routes of administration. The most used treatment in the US for the management of chronic *Pseudomonas* infection in subjects with CF is 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 FEV1 (forced expiratory volume in 1 second) of 25%-75%, has been sold in the US since January 1998. A 1999 study reported that Tobi, 300 mg, administered twice a day for cycles of 28 days followed by 28-days-off treatment was shown to reduce *Pseudomonas* colony counts, increase FEV1 percent predicted, reduce hospitalizations and decrease additional antibiotic use (Ramsey et al., 1999, 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 $500 million. We believe this market is being driven by physicians desire to maintain the lung function of CF patients, which continues to decline in many patients despite extensive treatment with current therapies including currently approved inhaled antibiotics. We believe that the following additional factors may lead to further market growth:

- Better patient adherence to physician prescribed regimens resulting from more convenient (less frequent and less time consuming) treatments;
- Physicians initiating treatment with inhaled antibiotics earlier for patients with *Pseudomonas* in their lungs;
- CF patients living longer;

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

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

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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 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 approximately 13 minutes per day for 28 days followed by a 28-day off-drug period. We believe that any inhaled treatment that reduces the treatment burden on a CF patient could represent a significant improvement in the patient s quality of life and result in improved compliance, as well as reduce the development of antibiotic resistance.

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 a sustained period of time, which we expect would differentiate it from other marketed drugs for the treatment of chronic *Pseudomonas* lung infections in CF patients. Current inhaled antibiotics are commonly used as standard treatments for CF patients with *Pseudomonas* lung infections and generally are thought to be a way to deliver more drug directly to the site of infection as compared with other methods of delivery. However, CF patients seldom clear the *Pseudomonas* permanently from their lungs, in part because of the thick sticky mucus these patients produce in their lungs, and often become chronically infected despite existing antibiotic treatments. All existing aminoglycoside antibiotics, including tobramycin and amikacin, are positively charged and tend to bind to the negative surfaces of mucus and the biofilm. In contrast, we have designed 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 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

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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

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 forced expiratory volume in one second (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;

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- 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 a 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. We expect to use this interim data from this study as part of our regulatory filings with the EMA and Health Canada, which we expect to submit during 2014, and 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.

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

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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 dog study, and there was no evidence of neoplasia, squamous metaplasia or proliferative changes.

We expect to reevaluate our plans regarding a US phase 3 clinical trial in CF patients with *Pseudomonas* lung infection after we receive the final results from the ongoing phase 2 clinical trial in NTM patients in the US.

Strategy for Commercialization

We currently plan to retain marketing rights for ARIKAYCE for CF patients with *Pseudomonas* lung infections in certain countries in Europe, Canada and the US. We believe ARIKAYCE will require a limited commercial infrastructure in these regions because of the small focused nature of the potential physician prescribing population for CF patients. We may seek to out-license ARIKAYCE in certain countries in Europe, as well as outside of Europe, Canada and the US.

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

Overview of Non-CF Bronchiectasis and Pseudomonas Lung Infections

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 *Pseudomonas* lung infections in CF patients and patients with NTM lung infections. We will evaluate our development and commercialization strategies for this indication when we complete our phase 2 study in patients with NTM infections.

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

Market

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

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become infected with *Pseudomonas*, they tend to have more frequent exacerbations and hospitalizations and are more frequent users of antibiotics.

Development Program

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

In May 2009 we completed our randomized, placebo controlled US phase 2 study (TR02-107) of 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 patient 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 do not intend to initiate further clinical studies with respect to a non-CF bronchiectasis indication until we have completed additional clinical studies for CF patients with *Pseudomonas* lung infections and for patients with NTM lung infections. Following those studies, we will evaluate whether to develop ARIKAYCE further for non-CF bronchiectasis.

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

Optimized eFlow Nebulizer System

If approved for commercialization, we expect that ARIKAYCE will be administered once daily via inhalation using an eFlow Nebulizer System optimized specifically for ARIKAYCE by PARI, a third-party vendor.

The optimized eFlow Nebulizer System is a medical device that uses PARI s patented eFlow technology to enable highly efficient delivery of inhaled medication, also called aerosolization, including liposomal formulations via a vibrating, perforated membrane that includes thousands of specially designed laser-drilled holes, which aids the delivery of ARIKAYCE to the lung. We believe the optimized eFlow Nebulizer System is state of the art and highly efficient. The eFlow Nebulizer System delivers a very high density of active drug, in a precisely defined and controlled droplet size, with a high proportion of respirable droplets delivered in a relatively short period of time. In addition, the eFlow Nebulizer System has a quiet mode of operation, is small in size, light weight and provides for optional battery-powered operation. We believe that using the eFlow Nebulizer System to deliver ARIKAYCE will

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reduce treatment time and ease the patient s treatment burden and thereby potentially improve patient compliance. We believe that improved compliance with the prescribed treatment regimen may lead to a reduction in the development of antibiotic resistance by increasing the exposure of the infection to the minimum inhibitory concentration of antibiotic and therefore may ultimately lead to clinical benefit.

MANUFACTURING OF ARIKAYCE

The ARIKAYCE used in our clinical studies is manufactured for us by Ajinomoto Althea, Inc. (Althea), a third-party contract manufacturing organization in the US. We are working with Althea to develop commercial production capabilities for ARIKAYCE. Our agreement with Althea provides for a term expiring in July 2014, subject to an earlier termination upon the provision of 180 days notice by either party, or in the event of an uncured material breach, certain bankruptcy or liquidation events, or upon the occurrence of certain other specified termination events. We are negotiating with Althea to extend the manufacture of ARIKAYCE at Althea beyond July 2014. There can be no assurance that we will enter into an agreement to extend the manufacture or that we will enter into an agreement on terms favorable to us.

In February 2014, we entered into a contract manufacturing agreement with Therapure for the manufacture of the Company s product ARIKAYCE at the larger scales necessary to support commercialization. Pursuant to the agreement, the Company and Therapure will collaborate to construct a production and quality control area for the manufacture and testing of ARIKAYCE in Therapure s existing manufacturing facility in Mississauga, Ontario, Canada. 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.

We are also exploring the possibility of establishing our own manufacturing facilities in order to support clinical studies and to support in the commercial launch of ARIKAYCE.

All sites of manufacture of ARIKAYCE use the technology developed and optimized by us. We and all our manufacturing partners must comply with applicable regulations relating to the current good manufacturing practices (cGMP) regulations of regulatory agencies. The cGMP regulations include requirements relating to the organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. We believe that all facilities will meet cGMP requirements for the sterile manufacturing of finished ARIKAYCE product.

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

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

IPLEX

In addition to the ARIKAYCE development program, we have a second proprietary compound, IPLEX®, which is IGF-1, with its natural binding protein, IGFBP-3. IPLEX is no longer a development priority for us. We no longer have protein development capability or the in-house capability to manufacture IPLEX. Previously, under the proprietary IPLEX protein platform, we maintained an expanded access program for amyotrophic lateral

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sclerosis (also known as ALS or Lou Gehrig s disease) until drug supplies were exhausted at the end of 2011. It is our intention to seek licensing partners for the IPLEX development programs. In 2012, we out-licensed the IPLEX technology to Premacure Holdings AB and Premacure AB of Sweden (collectively, Premacure) for retinopathy of prematurity indication. In March 2013, we amended the Premacure License Agreement to provide Premacure with the option to pay us $11.5 million and assume any of our royalty obligations to other parties in exchange for a fully paid license. In March 2013, Shire plc announced that they acquired Premacure. In April 2013 Shire exercised this option and paid us $11.5 million, and as a result we are not entitled to future royalties from Shire.

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

Since 2011, we have focused our development activities principally on our proprietary, advanced liposomal technology designed specifically for inhalation lung delivery. 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. In 2013, we completed a phase 3 trial in Europe and Canada in which we evaluated ARIKAYCE in CF patients with *Pseudomonas* lung infections. We are currently conducting two clinical trials: (1) the completion of the open-label portion of a phase 2 trial in the US in which we are evaluating ARIKAYCE for NTM infections and (2) 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 development expenses were for our ARIKAYCE program. We expect that our development efforts in 2014 will principally relate to the development of ARIKAYCE in the CF and NTM indications.

Our clinical trials with ARIKAYCE 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;

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- The number of clinical sites included in the trials;
- The length of time required to enroll suitable patient subjects; and
- The efficacy and safety profile of the product candidate.

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

General and Administrative Expenses

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

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, 2014 and 2013

Net Loss

Net loss for the three months ended March 31, 2014 was $14.3 million, or ($0.36) per common share basic and diluted, compared with a net loss of $13.7 million, or ($0.43) per common share basic and diluted for the three months ended March 31, 2013. The increase in our net loss in the first quarter of 2014 as compared to 2013 of $0.6 million was primarily due to:

- A $1.0 million increase in our research and development expenses that primarily resulted from an increase in internal expenses, specifically compensation and personnel related expenses, including non-cash stock compensation expense, and an increase in manufacturing expenses as a result of the completion of certain process improvement projects at our third party manufacturing partner and the manufacture of ARIKAYCE for clinical supply. These

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increases were offset by a decrease in external clinical expenses which was primarily related to the fact that our phase 3 pivotal study in CF patients was completed in 2013;

- A $2.8 million increase in our general and administrative expenses primarily resulted from an increase in pre-commercial activities, an increase in personnel costs due to an increase in headcount, and an increase in non-cash stock compensation expense; and

- A $3.2 million increase in the benefit from income taxes resulting from sale of a portion of our New Jersey State NOLs under the State of New Jersey s Technology Business Tax Certificate Transfer Program for cash of $4.4 million and $1.2 million in 2014 and 2013, respectively, and net of commissions.

Research and Development Expenses

Research and development expenses for the three months ended March 31, 2014 and 2013 comprised the following:

	Three Months Ended March 31,		Increase (Decrease)	
	2014	2013	$	%
External Expenses				
Clinical development	$ 3,084	$ 6,853	$	