AGIOS PHARMACEUTICALS INC
Form 10-Q
May 09, 2016
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 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, 2016

OR

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

Commission file number 001-36014

AGIOS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**26-0662915**
(State or Other Jurisdiction of	**(I.R.S. Employer**
Incorporation or Organization)	**Identification No.)**
88 Sidney Street, Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 649-8600

(Registrant s Telephone Number, Including Area Code)

(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

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

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

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

Large accelerated filer x	Accelerated filer ¨
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

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

Number of shares of the registrant s Common Stock, $0.001 par value, outstanding on May 5, 2016: 37,921,791

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AGIOS PHARMACEUTICALS, INC.

FORM 10-Q

FOR THE QUARTERLY PERIOD ENDED MARCH 31, 2016

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements (Unaudited).

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets

(in thousands, except share and per share data)

(Unaudited)

	March 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 39,035	$ 71,764
Marketable securities	273,859	245,238
Collaboration receivable related party	6,814	8,225
Tenant improvement and other receivables	571	3,374
Prepaid expenses and other current assets	9,190	8,728
Total current assets	329,469	337,329
Marketable securities	42,860	58,905
Property and equipment, net	22,950	23,220
Other assets	838	611
Total assets	$ 396,117	$ 420,065
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	$ 13,746	$ 14,748
Accrued expenses	12,247	15,996
Deferred revenue related party	16,523	19,665
Deferred rent	2,539	2,479
Total current liabilities	45,055	52,888
Deferred revenue, net of current portion related party	1,949	4,699
Deferred rent, net of current portion	16,740	17,360
Commitments and contingencies		
Stockholders equity:		
Preferred stock, $0.001 par value; 25,000,000 shares authorized; no shares issued or outstanding at March 31, 2016 and December 31, 2015		
	38	38

Common stock, $0.001 par value; 125,000,000 shares authorized; 37,899,242 and 37,696,502 shares issued and outstanding at March 31, 2016 and December 31, 2015, respectively		
Additional paid-in capital	640,124	630,078
Accumulated other comprehensive income (loss)	89	(318)
Accumulated deficit	(307,878)	(284,680)
Total stockholders equity	332,373	345,118
Total liabilities and stockholders equity	$ 396,117	$ 420,065

See accompanying notes to condensed consolidated financial statements.

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AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations

(in thousands, except share and per share data)

(Unaudited)

	Three Months Ended March 31,	
	2016	**2015**
Collaboration revenue related party	$ 31,281	$ 34,202
Operating expenses:		
Research and development (net of $8,794 and $4,366 of cost reimbursement from related party for the three months ended March 31, 2016 and 2015, respectively)	44,038	32,443
General and administrative	10,837	6,954
Total operating expenses	54,875	39,397
Loss from operations	(23,594)	(5,195)
Interest income	396	238
Net loss	$ (23,198)	$ (4,957)
Net loss per share basic and diluted	$ (0.61)	$ (0.13)
Weighted-average number of common shares used in net loss per share basic and diluted	37,864,084	37,214,747

See accompanying notes to condensed consolidated financial statements.

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AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Comprehensive Loss

(in thousands)

(Unaudited)

	Three Months Ended March 31,	
	2016	**2015**
Net loss	$ (23,198)	$ (4,957)
Other comprehensive income:		
Unrealized gain on available-for-sale securities	407	248
Comprehensive loss	$ (22,791)	$ (4,709)

See accompanying notes to condensed consolidated financial statements.

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AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows

(in thousands)

(Unaudited)

	Three Months Ended March 31,	
	2016	**2015**
Operating activities		
Net loss	$ (23,198)	$ (4,957)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	1,246	370
Stock-based compensation expense	9,107	5,060
Net amortization of premium and discounts on investments	126	172
Changes in operating assets and liabilities:		
Collaboration receivable related party	1,411	(524)
Tenant improvement and other receivables	2,803	(4,573)
Prepaid expenses and other assets	(857)	(708)
Accounts payable	(293)	(2,665)
Accrued expenses and other liabilities	(2,902)	1,574
Deferred rent	(560)	8,218
Refundable income taxes and income taxes payable		3,841
Deferred revenue related party	(5,892)	(31,393)
Net cash used in operating activities	(19,009)	(25,585)
Investing activities		
Purchases of marketable securities	(211,163)	(35,526)
Proceeds from maturities and sales of marketable securities	198,868	84,311
Purchases of property and equipment	(2,533)	(3,797)
Net cash (used in) provided by investing activities	(14,828)	44,988
Financing activities		
Payment of public offering costs		(207)
Net proceeds from stock option exercises and employee stock purchase plan	1,108	2,029
Net cash provided by financing activities	1,108	1,822
Net (decrease) increase in cash and cash equivalents	(32,729)	21,225
Cash and cash equivalents at beginning of the period	71,764	14,031
Cash and cash equivalents at end of the period	$ 39,035	$ 35,256

Supplemental disclosure of non-cash investing and financing transactions		
Additions to property, plant and equipment in accounts payable and accrued expenses	$ 607	$ 6,602
Vesting of restricted stock	$	$ 2
Proceeds from stock option exercises in other current assets	$ 17	$ 60

See accompanying notes to condensed consolidated financial statements.

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Agios Pharmaceuticals, Inc.

Notes to Condensed Consolidated Financial Statements

(Unaudited)

1. Overview and Basis of Presentation

Overview

Agios Pharmaceuticals, Inc. (Agios or the Company) is a biopharmaceutical company committed to the fundamental transformation of patients lives through scientific leadership in the field of cancer metabolism and rare genetic metabolic disorders. The Company has built a unique set of core capabilities in the field of cellular metabolism, with the goal of making transformative, first or best in class medicines. Agios therapeutic areas of focus are cancer and rare genetic metabolic disorders, which are a broad group of more than 600 rare genetic diseases caused by mutations, or defects, of single metabolic genes. In both of these areas, the Company is seeking to unlock the biology of cellular metabolism to create transformative therapies. The Company is located in Cambridge, Massachusetts.

Basis of presentation

The condensed consolidated interim balance sheet as of March 31, 2016, and the condensed consolidated interim statements of operations, comprehensive loss and cash flows for the three months ended March 31, 2016 and 2015, are unaudited. The unaudited condensed consolidated interim financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to present fairly the Company s condensed consolidated financial position as of March 31, 2016 and its results of operations and cash flows for the three months ended March 31, 2016 and 2015. The financial data and the other financial information disclosed in these notes to the condensed consolidated interim financial statements related to the three-month periods are also unaudited. The results of operations for the three months ended March 31, 2016 are not necessarily indicative of the results to be expected for the year ending December 31, 2016 or for any other future annual or interim period. The condensed consolidated interim financial statements should be read in conjunction with the audited consolidated financial statements and notes thereto included in the Company s Annual Report on Form 10-K for the year ended December 31, 2015 that was filed with the Securities and Exchange Commission (the SEC) on February 26, 2016.

The Company s consolidated financial statements include the Company s accounts and the accounts of the Company s wholly owned subsidiaries, Agios Securities Corporation and Agios International Sarl. All intercompany transactions have been eliminated in consolidation. The consolidated financial statements have been prepared in conformity with U.S. generally accepted accounting principles.

2. Summary of Significant Accounting Policies and Recent Accounting Pronouncements

Significant accounting policies

There have been no material changes to the significant accounting policies previously disclosed in the Annual Report on Form 10-K for the year ended December 31, 2015.

Recent accounting pronouncements

In April 2016, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing* (ASU 2016-10), which clarifies identifying performance obligation and licensing implementation guidance and illustrations in the ASU 2014-09, discussed below. ASU 2016-10 has the same effective date as the new revenue standard, ASU 2014-09, (as amended by the one-year deferral and the early adoption provisions in ASU 2015-14). In addition, entities are required to adopt the ASU by using the same transition method they used to adopt the new revenue standard. The Company is currently in the process of evaluating the impact of the guidance on its consolidated financial statements.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting* (ASU 2016-09), which simplifies several aspects of the accounting for employee share-based payment transactions, including income taxes consequences, classification of awards as either equity or liabilities, and classification in the statement of cash flows. ASU 2016-09 is effective for annual reporting periods beginning after December 15, 2016, including interim periods within those annual reporting periods. The Company is currently in the process of evaluating the impact of the guidance on its consolidated financial statements.

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In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net)* (ASU 2016-08), which amends the principal-versus-agent implementation guidance and illustrations in the ASU 2014-09, discussed below. ASU 2016-08 has the same effective date as the new revenue standard, ASU 2014-09, (as amended by the one-year deferral and the early adoption provisions in ASU 2015-14). In addition, entities are required to adopt the ASU by using the same transition method they used to adopt the new revenue standard. The Company is currently in the process of evaluating the impact of the guidance on its consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)* (ASU 2016-02), which establishes principles that lessees and lessors shall apply to report useful information to users of financial statements about the amount, timing and uncertainty of cash flows arising from a lease. ASU 2016-02 is effective for annual periods beginning after December 15, 2018 and interim periods therein, with early adoption permitted. The Company is currently in the process of evaluating the impact of the guidance on its consolidated financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements Going Concern (Subtopic 205-40)*. The ASU requires all entities to evaluate for the existence of conditions or events that raise substantial doubt about the entity s ability to continue as a going concern within one year after the issuance date of the financial statements. The accounting standard is effective for interim and annual periods ending after December 15, 2016 and will not have a material impact on the consolidated financial statements but may impact the Company s footnote disclosures.

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)*. The ASU provides for a single comprehensive model for use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance. The accounting standard is effective for interim and annual periods beginning after December 15, 2016 with no early adoption permitted. In April 2015, the FASB proposed a one year deferral of the effective date of this accounting update to annual periods beginning after December 15, 2017, along with an option to permit early adoption. The Company is required to adopt the amendments in the ASU using one of two acceptable methods. The Company is currently in the process of determining which adoption method it will apply and evaluating the impact of the guidance on its consolidated financial statements.

Other accounting standards that have been issued by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on the Company s financial statements upon adoption.

3. Fair Value Measurements

The Company records cash equivalents and marketable securities at fair value. Accounting Standards Codification (ASC) 820, *Fair Value Measurements and Disclosures*, establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company s own assumptions (unobservable inputs). The hierarchy consists of three levels:

Level 1 Unadjusted quoted prices in active markets for identical assets or liabilities.

Level 2 Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, directly or indirectly, for substantially the full term of the asset or liability.

Level 3 Unobservable inputs that reflect the Company s own assumptions about the assumptions market participants would use in pricing the asset or liability in which there is little, if any, market activity for the asset or liability at the

measurement date.

The following table summarizes the cash equivalents and marketable securities measured at fair value on a recurring basis as of March 31, 2016 (in thousands):

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	Level 1	Level 2	Level 3	Total
Cash equivalents	$ 26,845	$	$	$ 26,845
Marketable securities:				
Certificates of deposit		9,536		9,536
Government securities	216,672			216,672
Corporate debt securities		90,511		90,511
	$ 243,517	$ 100,047	$	$ 343,564

The following table summarizes the cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2015 (in thousands):

	Level 1	Level 2	Level 3	Total
Cash equivalents	$ 59,332	$	$	$ 59,332
Marketable securities:				
Certificates of deposit		11,243		11,243
Government securities	292,900			292,900
	$ 352,232	$ 11,243	$	$ 363,475

Cash equivalents and marketable securities have been initially valued at the transaction price and subsequently valued, at the end of each reporting period, utilizing third-party pricing services or other market observable data. The pricing services utilize industry standard valuation models, including both income and market based approaches and observable market inputs to determine value. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by the pricing services as of March 31, 2016 or December 31, 2015.

The carrying amounts reflected in the condensed consolidated balance sheets for cash, collaboration receivable related party, tenant improvement and other receivables, prepaid expenses and other current assets, other assets, accounts payable, and accrued expenses approximate their fair values at March 31, 2016 and December 31, 2015, due to their short-term nature.

There have been no changes to the valuation methods during the three months ended March 31, 2016 or 2015. The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between Level 1 and Level 2 during the three months ended March 31, 2016 or the year ended December 31, 2015. The Company had no financial assets or liabilities that were classified as Level 3 at any point during the three months ended March 31, 2016 or the year ended December 31, 2015.

4. Marketable Securities

Marketable securities at March 31, 2016 and December 31, 2015 consisted primarily of investments in certificates of deposit, government securities and corporate debt securities. Management determines the appropriate classification of the securities at the time they are acquired and evaluates the appropriateness of such classifications at each balance sheet date. The Company classifies its marketable securities as available-for-sale pursuant to ASC 320, *Investments Debt and Equity Securities*. Marketable securities are recorded at fair value, with unrealized gains and losses included as a component of accumulated other comprehensive loss in stockholders equity and a component of total comprehensive loss in the condensed consolidated interim statements of comprehensive loss, until realized. Realized

gains and losses are included in investment income on a specific-identification basis. There were no realized gains or losses on marketable securities for the three months ended March 31, 2016 and 2015.

Marketable securities at March 31, 2016 consist of the following (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
Certificates of deposit	$ 4,280	$ 1	$	$ 4,281
Government securities	204,639	53	(35)	204,657
Corporate debt securities	64,901	26	(6)	64,921
Non-current:				
Certificates of deposit	5,240	15		5,255
Government securities	12,019	3	(7)	12,015
Corporate debt securities	25,551	47	(8)	25,590
	$ 316,630	$ 145	$ (56)	$ 316,719

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Marketable securities at December 31, 2015 consist of the following (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
Certificates of deposit	$ 11,248	$	$ (5)	$ 11,243
Government securities	234,130	10	(145)	233,995
Non-current:				
Government securities	59,083		(178)	58,905
	$ 304,461	$ 10	$ (328)	$ 304,143

At March 31, 2016 and December 31, 2014, the Company held both current and non-current investments. Investments classified as current have maturities of less than one year. Investments classified as non-current are those that (i) have a maturity of one to two years and (ii) management does not intend to liquidate within the next twelve months, although these funds are available for use and therefore classified as available-for-sale.

The Company reviews marketable securities for other-than-temporary impairment whenever the fair value of a marketable security is less than the amortized cost and evidence indicates that a marketable security s carrying amount is not recoverable within a reasonable period of time. Other-than-temporary impairments of investments are recognized in the condensed consolidated interim statements of operations if the Company has experienced a credit loss, has the intent to sell the marketable security, or if it is more likely than not that the Company will be required to sell the marketable security before recovery of the amortized cost basis. Evidence considered in this assessment includes reasons for the impairment, compliance with the Company s investment policy, the severity and the duration of the impairment and changes in value subsequent to the end of the period.

At March 31, 2016 and December 31, 2015, the Company held 34 and 74 debt securities that were in an unrealized loss position for less than one year, respectively. The aggregate fair value of debt securities in an unrealized loss position at March 31, 2016 and December 31, 2015 was $101.6 million and $207.4 million, respectively. There were no individual securities that were in a significant unrealized loss position as of March 31, 2016 and December 31, 2015. The Company evaluated its securities for other-than-temporary impairment and considered the decline in market value for the securities to be primarily attributable to current economic and market conditions. It is not more likely than not that the Company will be required to sell the securities, and the Company does not intend to do so prior to the recovery of the amortized cost basis. Based on this analysis, these marketable securities were not considered to be other-than-temporarily impaired as of March 31, 2016 and December 31, 2015.

5. Collaboration Agreements

2010 Agreement and amendments

In April 2010, the Company entered into a collaboration agreement focused on cancer metabolism with Celgene Corporation, or Celgene, a related party through ownership of the Company s common stock. The agreement was amended in October 2011 and July 2014, as described below (the agreement together with the amendments, the 2010 Agreement). The goal of the collaboration is to discover, develop and commercialize disease-altering therapies in oncology based on the Company s cancer metabolism research platform. The Company will initially lead discovery, preclinical and early clinical development for all cancer metabolism programs under the collaboration.

The discovery phase of the 2010 Agreement was scheduled to expire in April 2014, subject to Celgene s option to extend the discovery phase for up to an additional two years with additional funding to the Company. In December 2013, Celgene elected to extend the term of the initial discovery phase from four years to five years, to April 2015, in exchange for the payment of a $20.0 million extension fee which was received in May 2014. In December 2014, Celgene elected to exercise its final option to extend the term of the initial discovery phase one additional year, to April 2016, in exchange for the payment of a $20.0 million extension fee which was received in May 2015. In April 2016, the Company reached an agreement with Celgene to defer from April 2016 to June 2016 the selection process for allocating the rights to certain discovery programs under the 2010 Agreement.

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Pursuant to the 2010 Agreement, the Company is responsible for nominating development candidates, of which two required confirmation by the Joint Research Committee (JRC) during the discovery phase. During the year ended December 31, 2012 the Company nominated its first development candidate (AG-221) and during the year ended December 31, 2013 the Company nominated its second development candidate (AG-120), both of which have been confirmed by the JRC pursuant to the 2010 Agreement. For each development candidate, Celgene elected to progress such development candidate into preclinical development, which required the Company to conduct studies to meet the requirements for filing an Investigational New Drug application (IND), or IND-enabling studies. Subsequently, the Company was required to file an IND for each of the two development candidates and, upon the FDA s acceptance of the INDs, Celgene requested that the Company conduct an initial phase 1 clinical trial relating to each of the two development candidates.

Celgene may elect to convert each discovery program for which the Company has nominated a development candidate into a co-commercialized licensed program, the attributes of which are described below. The Company has the right, exercisable during a specified period following FDA acceptance of the applicable IND, to convert one of every three co-commercialized licensed programs into a split licensed program, for which the Company will retain the United States rights, other attributes of which are further described below. In June 2014, Celgene exercised its option to an exclusive global license for the development and commercialization of the Company s isocitrate dehydrogenase 2 (IDH2) program, AG-221. The Company elected to retain U.S. rights to its isocitrate dehydrogenase 1 (IDH1) program, AG-120, in January 2014. Celgene exercised its rights under the 2010 Agreement to this program during the three months ended March 31, 2015. In addition, Celgene may license certain discovery programs that the Company does not nominate or the JRC does not confirm as a development candidate and for which Celgene will lead and fund global development and commercialization.

The July 2014 amendment of the 2010 Agreement allowed for more flexibility in the design and conduct of phase 1 clinical trials and additional nonclinical and/or clinical activities that the Company agreed to perform at Celgene s request. This amendment further modified the mechanism and timing for payments to be made with respect to such development activities.

Under the 2010 Agreement, the Company is eligible to receive up to $120.0 million in potential milestone payments payable for each program selected by Celgene. The potential milestone payments for each such program are comprised of: (i) a $25.0 million milestone payment upon achievement of a specified clinical development milestone event, (ii) up to $70.0 million in milestone payments upon achievement of specified regulatory milestone events, and (iii) a $25.0 million milestone payment upon achievement of a specified commercial milestone event. The Company is also eligible to receive additional milestone payments specific to co-commercialized licensed programs and split licensed programs. In addition, the Company is eligible to receive a substantive milestone payment of $22.5 million upon achievement of an early clinical development milestone event for certain co-commercialized licensed programs. Under the 2010 Agreement, in connection with the first split licensed program under the collaboration, the Company s IDH1 program, AG-120, the Company is eligible to receive an additional one-time payment of $25.0 million upon the dosing of the last patient in a Company-sponsored phase 2 clinical trial. In January 2016, the Company determined that a substantive clinical development milestone related to the AG-221 program was achieved and received a milestone payment of $25.0 million.

In addition to the milestone payments described above, for each co-commercialized licensed program, the Company will be reimbursed for all eligible development costs of the related phase 1 multiple ascending dose clinical trial. The initial costs will be reimbursed as a milestone payment equal to the greater of $5.0 million or eligible development costs incurred by the Company upon the earlier of the determination of the maximum tolerated dose or Celgene s election to license the program. Subsequent to the initial milestone payment, development costs will be reimbursed on a quarterly basis. In addition to the milestone payments described above, for each split licensed program, under the

2010 Agreement the Company is eligible for reimbursement of the costs of disease-specific expansion cohort(s) that support the initiation of a subsequent pivotal clinical trial. Costs will be reimbursed as a milestone payment equal to the lesser of $10.0 million or fifty percent of the eligible costs for the disease-specific expansion cohort(s) upon the first patient dosed under the pivotal clinical trial. Under the 2010 Agreement, the maximum amount for the milestone payment will be $10.0 million for each split licensed program regardless of the number of disease-specific expansion cohorts and pivotal trials undertaken for each split licensed program.

Under the 2010 Agreement, the Company may also receive royalties at tiered, low- to mid-teen percentage rates on net sales and has the option to participate in the development and commercialization of certain products in the United States. The royalty payments will be recognized as revenue in the period in which they are earned. To date, the Company has not earned any royalty payments under the 2010 Agreement.

Unless terminated earlier by either party, the term of the 2010 Agreement will continue until the expiration of the last-to-expire of all royalty terms with respect to all royalty-bearing products. Celgene may terminate this agreement for convenience in its entirety or with respect to one or more programs upon ninety days written notice to the Company. If either party is in material breach and fails to cure such breach within the specified cure period, the other party may terminate the 2010 Agreement in its entirety or with respect to one or more programs; however, if such breach relates solely to a specific program, the non-breaching party may only terminate the agreement with respect to such program. Either the Company or Celgene may terminate the agreement in the event of specified insolvency events involving the other party.

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AG-881 Agreements

On April 27, 2015, the Company entered into a joint worldwide development and profit share collaboration and license agreement with Celgene and the Company s wholly owned subsidiary, Agios International Sarl, entered into a collaboration and license agreement with Celgene International II Sarl (collectively, the AG-881 Agreements). The AG-881 Agreements establish a worldwide collaboration focused on the development and commercialization of AG-881 products. Under the terms of the AG-881 Agreements, the Company received an initial payment of $10.0 million in May 2015 and is eligible to receive milestone-based payments described below. The Company and Celgene will equally split all worldwide development costs, subject to specified exceptions, as well as any profits from any net sales of, or commercialization losses related to, licensed AG-881 products.

The Company is eligible to receive up to $70.0 million in potential milestone payments related to AG-881 under the AG-881 Agreements. The potential milestone payments are comprised of: (i) a $15.0 million milestone payment for filing of first NDA in a major market and (ii) up to $55.0 million in milestone payments upon achievement of specified regulatory milestone events. The Company may also receive royalties at tiered, low- to mid-teen percentage rates on net sales if it elects to not participate in the development and commercialization of AG-881.

Accounting analysis and revenue recognition collaboration revenue

Pre-July 2014

Prior to the July 2014 amendment of the 2010 Agreement, the Company concluded that none of the identified deliverables had stand-alone value and, therefore, accounted for the deliverables as a single unit of accounting. The Company further concluded it was unable to estimate the fair value of the undelivered items within the 2010 Agreement. All considerations were recognized on a straight-line basis through the period over which the Company expected to fulfill its performance obligations (the performance period), which was initially determined to be six years.

July 2014 April 2015

The July 2014 amendment was determined to be a material modification of the 2010 Agreement due to a change in the total potential consideration that was more than insignificant and changes to certain of the deliverables in the arrangement. Upon concluding the arrangement had been materially modified in July 2014, the Company identified the remaining deliverables under the arrangement and determined its best estimates of selling price for the undelivered elements as of the modification date as vendor specific objective evidence and third party evidence were not available. The Company then allocated the total arrangement consideration, which included the remaining deferred revenue balance at the modification date and other consideration that was deemed to be determinable at the modification date, to each unit of accounting based on its best estimate of selling price. The difference between the total arrangement consideration and the best estimate of selling price of the undelivered items was recognized as revenue at the modification date.

The undelivered items from the July 2014 modification, the related best estimate of selling price, the method of recognizing the allocated consideration, and the revenue recognized related to each unit of account for the three months ended March 31, 2015 was as follows:

License for the split licensed program AG-120: The Company developed the best estimate of selling price of the license by probability weighting multiple cash flow scenarios using the income approach. There were significant judgments and estimates inherent in the determination of the best estimate of selling price of this unit of accounting. Should different reasonable assumptions be utilized, the best estimate of selling price and the associated revenue recognized would be different. The Company allocated $21.2 million to the license which was delivered in January 2015. During the three months ended March 31, 2015, the Company recognized the non-contingent consideration allocated to this unit of accounting of $15.8 million as collaboration revenue.

Development services for five separate on-going phase 1 clinical trials (each of which is a separate unit of accounting): The Company developed the best estimate of selling price of the on-going phase 1 clinical trial development services of $50.8 million for all five studies using management s best estimate of the cost of obtaining these services at arm s length from a third-party provider, as well as internal full time equivalent costs to support the development services. The amount allocated to these units of accounting is recognized as revenue on a proportional performance basis as services are provided. As committed to on the date of the July 2014 amendment, the Company has completed services for three of the on-going phase 1 clinical trials and expected services for the remaining two on-going phase 1 clinical trials are expected to be performed

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through the second quarter of 2016. As additional consideration is earned and allocated to the three fully delivered units of accounting it is recognized immediately. During the three months ended March 31, 2015 the Company recognized the non-contingent consideration allocated to these units of accounting of $14.3 million as collaboration revenue.

On-going research and development: The Company developed the best estimate of selling price of the research and development services of $13.6 million using management s best estimate of the cost of obtaining these services at arm s length from a third-party provider. The amount allocated to this unit of accounting was recognized as revenue ratably over the performance period. During the three months ended March 31, 2015 the Company recognized the non-contingent consideration allocated to this unit of accounting of $4.0 million as collaboration revenue.

Committee participation: The Company developed the best estimate of selling price of the committee participation services of $0.2 million using management s best estimate of the anticipated participation hours multiplied by a market rate for comparable participants. The amount allocated to this unit of accounting was recognized as revenue ratably over the performance period. During the three months ended March 31, 2015 the Company recognized the non-contingent consideration allocated to this unit of accounting of $0.1 million as collaboration revenue.

In December 2014, Celgene elected to extend the term of the discovery period over which the Company was providing on-going research and development services from five to six years, to April 2016. As a result of the extension, the Company received a $20.0 million extension payment from Celgene in May 2015. The Company evaluated the extension and concluded that upon exercise it is obligated to provide its committee participation and research and development services for a period of one year from April 2015 through April 2016, and as such revenue should be recognized ratably over the performance period of April 2015 to April 2016 as services are rendered. The Company did not recognize any revenues related to the extension during the three months ended March 31, 2015.

Beginning in the first quarter of 2015, the Company and Celgene agreed to plans to advance AG-221 into later stage development studies. Pursuant to the terms of the 2010 Agreement, the parties agreed to transition primary development responsibilities for AG-221 to Celgene for later stage development at which point Celgene became the lead development party for AG-221. During the transition, the Company continued to manage certain arrangements with third-party service providers whose contracts were assigned to Celgene. The Company determined it is no longer the primary obligor of these arrangements and, when considering the other factors included within ASC 605-45, *Revenue Recognition Principal Agent Considerations*, determined reimbursement of amounts incurred under third-party contracts should be reported on a net basis within research and development expense. The Company re-assessed its estimate of the total level of effort required to perform the development services related to AG-221 as a result of the contract assignments and recorded a change in estimate during the three months ended March 31, 2015. This change in estimate resulted in the recognition of an additional $5.1 million of revenue, which is included within revenue related to development services for five separate on-going phase 1 clinical trials discussed earlier within this footnote. Including the $3.8 million presented as a reduction of research and development expenditures, the change in estimate reduced the Company s net loss by $8.9 million and caused a decrease in net loss per share of $0.24 during the three months ended March 31, 2015.

During the period January 1, 2015 through April 27, 2015, the execution date of the AG-881 Agreements, the Company performed planning services on behalf of Celgene related to an expanded phase 1 clinical trial of AG-221. The Company determined the work represented a substantive option under the 2010 Agreement. The Company also determined it is not the primary obligor of the underlying third-party contracts and determined that reimbursements of

amounts incurred under the contracts should be reported on a net basis in research and development expense. Reimbursements of services performed directly by the Company are presented on a gross basis as collaboration revenue. During the three months ended March 31, 2015, the Company recognized $0.1 million in revenue and recorded $0.6 million as a reduction in research and development costs related to these services.

Post-April 2015

The AG-881 Agreements, executed on April 27, 2015, were determined to be a modification of the 2010 Agreement due to the AG-881 Agreements including a compound originally identified within the 2010 Agreement. As a result of the modification the Company identified the remaining deliverables under the 2010 Agreement and the AG-881 Agreements with Celgene and determined the best estimate of selling price for the undelivered elements as of the modification date. The Company then allocated the total arrangement consideration, which included the remaining deferred revenue balance at the modification date, the initial payment of $10.0 million under the AG-881 Agreements and other consideration under the 2010 Agreement and the AG-881 Agreements that was deemed to be determinable at the modification date, to each unit of accounting relative to its best estimate of selling price. The undelivered items, which are each considered by the Company to have stand-alone value and therefore are separate units of accounting, the related best estimate of selling price at April 27, 2015, and the method of recognizing the allocated consideration, for each unit of accounting are as follows:

Licenses for the AG-881 program: The Company developed the best estimate of selling price of the U.S. license and the rest of world license by probability weighting multiple cash flow scenarios using the income approach. Management estimates within the models include the expected, probability-weighted net profits from estimated future sales, an estimate

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of the direct cost incurred to generate future cash flows, a discount rate and other business forecast factors. There are significant judgments and estimates inherent in the determination of the best estimate of selling price of these units of accounting. These judgments and estimates include assumptions regarding future operating performance, the timelines of the clinical trials and regulatory approvals and the estimated patient populations. Should different reasonable assumptions be utilized, the best estimate of selling price and the associated revenue recognized would be different. The Company developed a best estimate of selling price of the licenses of $33.2 million. The Company recognizes the non-contingent consideration allocated to these units of accounting upon delivery of the licenses to Celgene which occurred immediately upon the execution of the AG-881 Agreements. During the three months ended March 31, 2016, the Company recognized the non-contingent consideration allocated to this unit of accounting of $0.9 million as collaboration revenue.

Four separate on-going development services for which the Company determined it is acting as the principal of all development activities (each of which is a separate unit of accounting): The Company developed the best estimate of selling price for all four of the on-going development services of $12.7 million using management s best estimate of the cost of obtaining these services at arm s length from a third-party provider, as well as internal full time equivalent costs to support the development services. The estimated costs were determined to represent management s best estimate of the price these services could be sold for separately. The amount allocated to these units of accounting is being recognized as revenue on a proportional performance basis as services are provided. The Company expects the services to be performed through 2017. When considering the factors included within ASC 605-45, the Company determined it is the principal of all development activities and is required to present reimbursement of amounts incurred for these services as revenue. During the three months ended March 31, 2016, the Company recognized the non-contingent consideration allocated to these units of accounting of $1.0 million as collaboration revenue.

Four separate on-going development services for which the Company determined it is not acting as the principal of all development activities (each of which is a separate unit of accounting): The Company developed the best estimate of selling price for all four of the on-going development services of $97.3 million using management s best estimate of the cost of obtaining these services at arm s length from a third-party provider, as well as internal full time equivalent costs to support the development services. The estimated costs were determined to represent management s best estimate of the price these services could be sold for separately. The amount allocated to these units of accounting is being recognized on a proportional performance basis as services are provided. The Company expects the services to be performed through 2017. When considering the factors included within ASC 605-45, the Company determined it is not the principal of all development activities and is required to present reimbursement of amounts incurred for these services on a net basis as a reduction of research and development expenses. During the three months ended March 31, 2016, the Company recognized the non-contingent consideration allocated to these units of accounting of $4.8 million as a reduction of research and development costs related to these services.

On-going research and development: The Company developed the best estimate of selling price of the research and development services of $30.5 million using management s best estimate of the cost of obtaining these services at arm s length from a third-party provider. The amount allocated to this unit of accounting is being recognized as revenue ratably over the performance period through April 2016. For the three months ended March 31, 2016, the Company recognized the non-contingent consideration allocated to this unit of accounting of $3.6 million as collaboration revenue.

Committee participations under the 2010 Agreement and AG-881 Agreements: The Company developed the best estimate of selling price of the committee participation services of $0.8 million using management s best estimate of the anticipated participation hours multiplied by a market rate for comparable participants. The amount allocated to this unit of accounting is being recognized as revenue ratably over the performance period, through the fourth quarter of 2016. During the three months ended March 31, 2016, the Company recognized the non-contingent consideration allocated to this unit of accounting of $0.1 million as collaboration revenue.

The total estimated arrangement consideration, as well as the expected timing of revenue recognition, is adjusted based on changes in estimated arrangement consideration as a result of changes in estimate for on-going development services. The allocable consideration will increase as the Company performs certain services for which it is eligible to receive additional consideration. These amounts will be recognized on a cumulative catch-up basis for any in-process units of accounting or immediately for any fully delivered units of accounting. The estimated arrangement consideration may decrease if the Company receives less reimbursement than initially estimated.

As a result of Celgene assuming the primary development responsibilities for AG-221 in the first quarter of 2015, the Company recorded $0.5 million of third party costs incurred on behalf of Celgene during the three months ended March 31, 2016 as a reduction of research and development costs.

Beginning in the third quarter of 2015, the Company initiated a phase 1b frontline combination clinical trial of AG-221 and AG-120 for which it will receive reimbursement from Celgene. The new combination trial was determined to be a substantive option under the

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2010 Agreement. When considering the factors included within ASC 605-45, management determined that the Company is the principal for the efforts related to the AG-221 arm of the combination trial but is acting in the role of an agent for the efforts related to the AG-120 arm of the combination trial. Accordingly, consideration earned related to the AG-221 arm of the combination trial is recognized as collaboration revenue in the period earned and consideration earned related to the AG-120 arm of the combination trial is reported as a reduction of research and development expense in the period earned. During the three months ended March 31, 2016, the Company recognized $0.7 million in collaboration revenue and recorded $0.2 million as a reduction of research and development costs related to the combination trial.

During the three months ended March 31, 2016, the Company incurred an additional $2.8 million and $0.5 million in reimbursable development expenses related to the AG-120 and AG-881 programs, respectively, that was not contemplated as of the April 2015 modification. The amounts are recorded as a reduction of research and development costs of each respective program.

During the three months ended March 31, 2016 and 2015, the Company recognized a total of $6.3 million and $34.2 million, respectively, as collaboration revenue and recognized $8.8 million and $4.4 million, respectively, as a reduction of research and development expenses.

In determining the current and noncurrent classification of deferred revenue, the Company considers the total consideration expected to be earned in the next twelve months for services to be performed under certain units of accounting and the estimated proportional performance and timing of delivery of certain deliverables to determine the deferred revenue balance that will remain twelve months from the balance sheet date. As of March 31, 2016 and December 31, 2015, the Company has recorded a collaboration receivable of $6.8 million and $8.2 million, respectively, related to reimbursable development costs.

Accounting analysis and revenue recognition milestone revenue

The Company concluded that certain of the clinical development and regulatory milestone payments that may be received under the 2010 Agreement and the AG-881 Agreements, if the Company is involved in future product development and commercialization, are substantive. Factors considered in the evaluation of the milestones included the degree of risk associated with performance of the milestone, the level of effort and investment required, whether the milestone consideration was reasonable relative to the deliverables and whether the milestone was earned at least in part based on the Company s performance. Revenue from substantive milestones, if they are nonrefundable, are recognized as revenue upon successful accomplishment of the milestones. Clinical and regulatory milestones are deemed non-substantive if they are based solely on the collaborator s performance. Non-substantive milestones will be recognized when achieved to the extent the Company has no remaining performance obligations under the arrangement. Milestone payments earned upon achievement of commercial milestone events will be recognized when earned.

In January 2016, the Company determined that a substantive clinical development milestone related to the AG-221 program was achieved and received a milestone payment of $25.0 million, which was recognized as revenue during the three months ended March 31, 2016.

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	March 31, 2016	December 31, 2015
Accrued compensation	$ 3,451	$ 7,005
Accrued contracted research and development costs	7,404	7,449
Accrued professional fees	1,126	228
Accrued other	266	1,314
Total	$ 12,247	$ 15,996

7. Share-Based Payments

2013 Stock Incentive Plan

In June 2013, the Company s Board of Directors adopted and, in July 2013, the Company s stockholders approved the 2013 Stock Incentive Plan (the 2013 Plan). The 2013 Plan became effective upon the closing of the Company s Initial Public Offering, or IPO, and provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-

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based awards. Following the adoption of the 2013 Plan, the Company granted no further stock options or other awards under the 2007 Stock Incentive Plan, or 2007 Plan. Any options or awards outstanding under the 2007 Plan at the time of adoption of the 2013 Plan remain outstanding and effective. As of March 31, 2016, the total number of shares reserved under the 2007 Plan and the 2013 Plan are 6,676,545, and the Company had 1,169,125 shares available for future issuance under such plans. The 2013 Plan provides for an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2014 and continuing until the expiration of the 2013 Plan, equal to the lesser of (i) 2,000,000 shares of common stock, (ii) 4% of the outstanding shares of common stock on such date or (iii) an amount determined by the Company s Board of Directors. On January 1, 2016 and 2015, the annual increase for the 2013 Plan resulted in an additional 1,507,860 shares and 1,484,020 shares, respectively, authorized for issuance.

The following table summarizes all stock option activity for the three months ended March 31, 2016:

	Number of Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2015	4,618,697	$ 44.45	7.49	$ 153,573
Granted	937,665	40.87		
Exercised	(190,413)	2.82		
Forfeited/expired	(47,599)	75.17		
Outstanding at March 31, 2016	5,318,350	$ 45.03	7.76	$ 72,522
Exercisable at March 31, 2016	2,285,769	$ 23.13	6.23	$ 58,510
Vested and expected to vest at March 31, 2016	4,956,261	$ 45.40	7.72	$ 67,184

The weighted-average grant date fair value of options granted was $26.08 and $68.60 during the three months ended March 31, 2016 and 2015, respectively. The total intrinsic value of options exercised was $10.0 million and $18.2 million during the three months ended March 31, 2016 and 2015, respectively.

At March 31, 2016, the total unrecognized compensation expense related to unvested stock option awards, including estimated forfeitures, was $99.4 million, which the Company expects to recognize over a weighted-average period of approximately 2.9 years. The Company also has unrecognized stock-based compensation expense of $8.2 million related to stock options and performance-based stock units with performance-based vesting criteria that are not considered probable of achievement as of March 31, 2016.

Restricted stock units

The Company may grant awards of restricted stock units (RSUs) to non-employee directors, members of the management team and employees on a discretionary basis pursuant to the 2013 Plan. Each RSU entitles the holder to receive, at the end of each vesting period, a specified number of shares of the Company s common stock.

During the three months ended March 31, 2016, the Company granted 58,800 RSUs to various employees; no RSUs were granted during the three months ended March 31, 2015. The Company recorded stock-based compensation expense related to RSUs of $0.4 million and $0.1 million for the three months ended March 31, 2016 and 2015, respectively. These amounts are included in the total stock-based compensation expense disclosed below. As of March 31, 2016, there was approximately $3.1 million of total unrecognized compensation expense related to RSUs, which is expected to be recognized over a weighted-average period of 1.7 years.

The following table presents RSU activity for the three months ended March 31, 2016:

	Number of Stock Units	Weighted-average grant date fair value
Unvested shares at December 31, 2015	15,000	$ 122.22
Granted	58,800	39.76
Vested		
Unvested shares at March 31, 2016	73,800	$ 56.52

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Performance-based stock options

During the three months ended March 31, 2016 and 2015, no options to purchase shares of common stock that contain performance-based or a combination of performance-based and service-based vesting criteria were granted by the Company. However, certain performance-based stock options issued in prior periods were still outstanding as of March 31, 2016. Performance-based vesting criteria for options primarily relate to milestone events specific to the Company s corporate goals, including but not limited to certain preclinical and clinical development milestones related to the Company s product candidates. Stock-based compensation expense associated with these performance-based stock options is recognized if the performance condition is considered probable of achievement using management s best estimates. As of March 31, 2016, certain of the performance-based milestones had been achieved. The achievements of certain other milestones have been deemed probable and therefore the related expense either has been fully recognized or is being recognized over the remaining service period. The achievement of the remaining milestones was deemed to be not probable as of March 31, 2016 and, therefore, no expense has been recognized related to these awards. During the three months ended March 31, 2015, the Company recognized stock-based compensation expense of $0.1 million related to stock options with performance-based vesting criteria. During the three months ended March 31, 2016, the Company did not recognize any stock-based compensation expense related to stock options with performance-based vesting criteria.

Performance-based stock units

In December 2015, pursuant to the 2013 Plan, the Company granted 100,270 performance stock units (PSUs) to certain employees and, in February 2016, the Company granted 15,000 PSUs to one employee. Each PSU entitles the holder to receive, at the achievement of the performance-based and service-based criteria, a specified number of shares of the Company s stock. Performance-based vesting criteria primarily relate to milestone events specific to the Company s corporate goals, specifically regulatory development milestones related to the Company s product candidates. Stock-based compensation expense associated with these PSUs is recognized if the performance condition is considered probable of achievement using management s best estimates. As of March 31, 2016, these milestones were not probable and, therefore, no expense has been recognized related to these awards. No such awards were granted during the three months ended March 31, 2015.

2013 Employee Stock Purchase Plan

In June 2013, the Company s Board of Directors adopted, and in July 2013 the Company s stockholders approved, the 2013 Employee Stock Purchase Plan (the 2013 ESPP). The 2013 ESPP is administered by the Company s Board of Directors or by a committee appointed by the Company s Board of Directors. Under the 2013 ESPP, each offering period is six months, at the end of which employees may purchase shares of common stock through payroll deductions made over the term of the offering period. The per-share purchase price at the end of each offering period is equal to 85% of the closing price of one share of the Company s common stock at the beginning or end of the offering period, whichever is lower, subject to Internal Revenue Service limits. The Company issued 12,327 shares and 10,664 shares during the three months ended March 31, 2016 and 2015, respectively, under the 2013 ESPP. The 2013 ESPP provides participating employees with the opportunity to purchase up to an aggregate of 327,272 shares of the Company s common stock. As of March 31, 2016, the Company had 297,795 shares available for future issuance under the 2013 ESPP.

The Company recorded $0.1 million of stock-based compensation expense for the each of the three months ended March 31, 2016 and 2015, respectively, related to the 2013 ESPP.

Stock-based compensation expense

During the three months ended March 31, 2016 and 2015, the Company recorded stock-based compensation expense for employee and non-employee stock options, restricted stock units, restricted stock, performance-based stock options, performance-based stock units and the employee stock purchase plan shares. Expenses related to these equity-based awards were allocated as follows in the condensed consolidated interim statements of operations (in thousands):

	Three Months Ended March 31,	
	2016	2015
Research and development expense	$ 5,528	$ 2,611
General and administrative expense	3,579	2,449
	$ 9,107	$ 5,060

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The fair value of each stock option granted to employees is estimated on the date of grant using the Black-Scholes option-pricing model. For non-employees, the fair value of each stock option is estimated on each vesting and reporting date using the Black-Scholes option-pricing model. The following table summarizes the weighted average assumptions used in calculating the grant date fair value of the awards:

	Three Months Ended March 31,	
	2016	2015
Risk-free interest rate	1.42%	1.71%
Expected dividend yield		
Expected term (in years)	6.08	6.08
Expected volatility	71.53%	70.35%

8. Income Taxes

In January 2014, the Company paid $6.0 million as payment in full of its U.S. federal income tax liability related to the year ended December 31, 2011, including $1.5 million of interest and penalties accrued. The Company filed a carryback claim to apply the net losses incurred during the year ended December 31, 2013 against the previous taxable income. The amount to be refunded by the Internal Revenue Service (IRS) was recorded as refundable income taxes as of December 31, 2014. During the three months ended March 31, 2015, the Company received the balance of the refundable income tax. There was no (benefit) provision for income taxes during the three months ended March 31, 2016 and 2015.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. The Company evaluated whether any uncertain tax positions arise from commencing operations of its wholly owned subsidiary, Agios International Sarl, and determined no uncertain tax positions existed. As of March 31, 2016 and December 31, 2015, the Company did not have any uncertain tax positions.

9. Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the dilutive net loss per share calculation, stock options, restricted stock units, unvested restricted stock and employee stock purchase plan options are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share as their effect would be anti-dilutive; therefore, basic and diluted net loss per share were the same for all periods presented.

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Three Months Ended March 31,	
	2016	2015

Stock options	5,318,350	4,543,028
Restricted stock units	73,800	10,000
Unvested restricted stock		5,681
Employee stock purchase plan options	4,227	1,125
	5,396,377	4,559,834

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Item 2. Management s Discussion and Analysis of Financial Condition and Results of Operations.

Forward-looking Information

The following discussion of our financial condition and results of operations should be read with our unaudited condensed consolidated interim financial statements as of March 31, 2016 and for the three months ended March 31, 2016 and 2015 and related notes included in Part I. Item 1 of this Quarterly Report on Form 10-Q, as well as the audited consolidated financial statements and notes and Management s Discussion and Analysis of Financial Condition and Results of Operations and Risk Factors, included in our Annual Report on Form 10-K for the year ended December 31, 2015 filed with the Securities and Exchange Commission, or the SEC, on February 26, 2016. This Management s Discussion and Analysis of Financial Condition and Results of Operations contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on current expectations, estimates, forecasts, and projections and the beliefs and assumptions of our management and include, without limitation, statements with respect to our expectations regarding our research, development and commercialization plans and prospects, results of operations, general and administrative expenses, research and development expenses, and the sufficiency of our cash for future operations. Words such as anticipate, believe, estimate, expect, intend, may, plan, predict, project, target, potential, will, would, similar statements or variation of these terms or the negative of those terms and similar expressions are intended to identify these forward-looking statements. Readers are cautioned that these forward-looking statements are predictions and are subject to risks, uncertainties, and assumptions that are difficult to predict. Therefore, actual results may differ materially and adversely from those expressed in any forward-looking statements. Among the important factors that could cause actual results to differ materially from those indicated by our forward-looking statements are those discussed under the heading Risk Factors in Part II, Item 1A and elsewhere in this report. We undertake no obligation to revise the forward-looking statements contained herein to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events.

Overview

We are a biopharmaceutical company committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and rare genetic metabolic disorders, or RGDs, which are a subset of orphan genetic metabolic diseases. Metabolism is a complex biological process involving the uptake and assimilation of nutrients in cells to produce energy and facilitate many of the processes required for cellular division and growth. We focus our efforts on using cellular metabolism, an unexploited area of biological research with disruptive potential, as a platform for developing potentially transformative small molecule medicines. Our most advanced cancer product candidates are AG-221 and AG-120, which target mutated isocitrate dehydrogenase 2 and 1, or IDH2 and IDH1, respectively, and AG-881, which targets both mutated IDH1 and mutated IDH2. These mutations are found in a wide range of hematological malignancies and solid tumors. The lead product candidate in our RGD programs, AG-348, targets pyruvate kinase-R for the treatment of pyruvate kinase deficiency. Pyruvate kinase deficiency is a rare disorder that often results in severe hemolytic anemia due to inherited mutations in the pyruvate kinase enzyme within red blood cells.

In April 2010, we entered into a discovery and development collaboration and license agreement, or the 2010 Agreement, with Celgene Corporation, or Celgene, focused on targeting cancer metabolism. The goal of the collaboration under the 2010 Agreement is to discover, develop and commercialize disease-altering therapies in oncology arising out of our cancer metabolism research platform that have achieved development candidate status. On December 8, 2014, Celgene elected to extend the period of its exclusivity for an additional year to April 2016. The extension marked the final year of the discovery phase. We received a $20.0 million payment as a result of the extension in May 2015. In April 2016, we reached an agreement with Celgene to defer from April 2016 to June 2016 the selection process for allocating the rights to certain discovery programs under the 2010 Agreement.

Under the terms of the 2010 Agreement, we lead research, preclinical and early development efforts through phase 1, while Celgene received an option to obtain exclusive rights either upon Investigational New Drug application, or IND, acceptance or at the end of phase 1 to further develop and commercialize medicines emerging from our cancer metabolism research. Celgene would lead and fund global development and commercialization of development candidates for which it exercises its option to obtain a co-commercialization license, and we would retain development and commercialization rights in the United States for development candidates for which we exercise our option to retain a split license. On all programs under the 2010 Agreement for which Celgene exercises its option, we are eligible to receive up to $120.0 million in milestone-based payments as well as royalties on any sales.

We nominated AG-221 and AG-120 during the discovery phase of the collaboration under the 2010 Agreement. In June 2014, Celgene exercised its exclusive option to license worldwide development and commercialization rights for AG-221. In addition to contributing our scientific and translational expertise, we continue to conduct certain clinical development and regulatory activities within the AG-221 development program while transitioning responsibilities to Celgene, which will lead later development activities. Celgene exercised its exclusive option under the 2010 Agreement to license development and commercialization rights to AG-120 outside the United States during the three months ended March 31, 2015. Following Celgene s exercise of this option, we retained development and commercialization rights for AG-120 in the United States.

During April 2015, we selected a third novel IDH mutant inhibitor, AG-881, for clinical development. On April 27, 2015, we entered into a joint worldwide development and profit share collaboration and license agreement with Celgene and our wholly owned subsidiary, Agios International Sarl, which was organized in Switzerland in April 2015, entered into a collaboration and license agreement with Celgene International II Sarl. We refer to these agreements collectively as the AG-881 Agreements. The AG-881 Agreements establish a worldwide collaboration focused on the development and commercialization of AG-881 products. Under the terms of the AG-881 Agreements, we received initial upfront payments totaling $10.0 million in May 2015 and are eligible to receive up to $70.0 million in milestone-based payments. We and Celgene will equally split all worldwide development costs, subject to specified exceptions, as well as any profits from any net sales of, or commercialization losses related to, licensed AG-881 products.

Since inception, our operations have focused on organizing and staffing our company, business planning, raising capital, assembling our core capabilities in cellular metabolism, identifying potential product candidates, undertaking preclinical studies and conducting

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clinical trials. To date, we have financed our operations primarily through funding received from the 2010 Agreement, the AG-881 Agreements, private placements of our preferred stock, our initial public offering of our common stock and concurrent private placement of common stock to an affiliate of Celgene and our follow-on public offerings. Substantially all of our revenue to date has been collaboration revenue received from Celgene.

Since inception, we have incurred significant operating losses. Our net loss was $23.2 million and $5.0 million for the three months ended March 31, 2016 and 2015, respectively. As of March 31, 2016, we had an accumulated deficit of $307.9 million. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from year to year. We anticipate that our expenses will increase significantly as we continue to advance and expand clinical development activities for our lead programs, AG-221, AG-120, AG-881 and AG-348, as well as AG-519 our second product candidate that is a potent activator of the PKR enzyme; continue to discover and validate novel targets and drug product candidates; expand and protect our intellectual property portfolio; and hire additional commercial, development and scientific personnel.

Financial Operations Overview

Revenue

Through March 31, 2016, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales in the near future. Primarily all of our revenue to date has been derived from our collaborations with Celgene. In the future, we will seek to generate revenue from a combination of product sales and upfront payments, cost reimbursements, milestone payments, and royalties on future product sales.

Collaboration and license revenue

Arrangement consideration is allocated to each separately identified unit of accounting based on the relative selling price, using our best estimate of selling price of each deliverable. The provisions of the Financial Accounting Standards Board s Accounting Standards Codification (ASC) 605-25, *Multiple-Element Arrangements* are then applied to each unit of accounting to determine the appropriate revenue recognition. In the event that a deliverable of a multiple element arrangement does not represent a separate unit of accounting, we recognize revenue from the combined units of accounting over the term of the related contract or as undelivered items are delivered, as appropriate.

Revenue is recognized under the proportional performance method for certain units of accounting. The amount recognized is determined based on the consideration allocated to each unit of accounting based on the ratio of the level of effort incurred to date compared to the total estimated level of effort required to complete our performance obligations under the unit of accounting. Determining the total estimated level of effort required to complete all performance obligations requires management judgment and estimation, including assumptions regarding future operating performance, the timelines of the clinical trial approvals and the estimated patient populations.

Reimbursement of research and development costs by Celgene is recognized as revenue, provided we have determined that we are acting primarily as a principal in the transaction according to the provisions outlined in ASC 605-45, *Revenue Recognition Principal Agent Considerations*, the amounts are determinable and collection of the related receivable is reasonably assured.

Milestone revenue

We recognize revenue contingent upon the achievement of a milestone in its entirety in the period in which the milestone is achieved, only if the milestone meets all the criteria within the guidance to be considered substantive. At the inception of each arrangement that includes milestone payments, we evaluate each contingent payment on an individual basis to determine whether they are considered substantive milestones, specifically reviewing factors such as the degree of certainty in achieving the milestone, the research and development risk and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity s performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity s performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement.

Revenue from milestones, if they are nonrefundable and deemed substantive, are recognized upon achievement of the milestones. We recognize revenue associated with the non-substantive milestones upon achievement of the milestone if there are no undelivered elements and we have no remaining performance obligations.

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Research and development expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our product candidates, which include:

- employee-related expenses including salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research and development and both preclinical and clinical activities on our behalf and the cost of consultants;
- the cost of lab supplies and acquiring, developing and manufacturing preclinical and clinical study materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other operating costs.

Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed. Reimbursements received from Celgene for certain third-party costs for which we are not the principal in the transaction according to the provisions of ASC 605-45 are recorded as a reduction to research and development expense.

The following summarizes our most advanced current research and development programs.

AG-221: lead IDH2 program

AG-221 is an orally available, selective, potent inhibitor of the mutated IDH2 protein, making it a highly targeted therapeutic candidate for the treatment of patients with cancers that harbor IDH2 mutations, including those with acute myeloid leukemia, or AML, who have a historically poor prognosis. On June 16, 2014, the U.S. Food and Drug Administration, or FDA, granted us orphan drug designation for AG-221 for treatment of patients with AML. On August 13, 2014, we announced that the FDA granted fast track designation to AG-221 for treatment of patients with AML that harbor an IDH2 mutation. In April 2016, we and Celgene received European Medicines Agency, or EMA, Orphan Drug Designation for AG-221 for the treatment of AML. We have been evaluating AG-221 in several phase 1 dose-escalation clinical trials evaluating both hematological and solid tumor cancers with IDH2 mutations. To date, all clinical data reported by us in hematological cancers highlights that the mechanism of response is consistent with preclinical studies, including substantial reduction of plasma 2-hydroxygluturate, or 2HG, levels, as well as evidence of cellular differentiation and normalization of cell counts in the bone marrow and blood. This differentiation effect is distinct from that seen with traditional chemotherapeutics commonly used to treat AML.

In September 2013, we initiated our first phase 1 multicenter, open-label, dose-escalation clinical trial to assess the safety, clinical activity, and tolerability of AG-221 in patients with advanced hematologic malignancies with an IDH2 mutation. In June 2014, Celgene exercised its option to an exclusive global license for development and commercialization of AG-221 under a collaboration agreement between us and Celgene, which focuses on cancer

metabolism, or the 2010 Agreement. Under the 2010 Agreement, Celgene is responsible for all development costs for AG-221. We are eligible to receive up to $120.0 million in milestone payments and a tiered royalty on any net sales of products containing AG-221. In January 2016, in conjunction with the initiation of AG-221 phase 3 trials we received a milestone payment of $25.0 million. We also have the right to conduct a portion of any commercialization activities for AG-221 in the United States. In addition to contributing our scientific and translational expertise, we will continue to conduct some clinical development and regulatory activities within the AG-221 development program in collaboration with Celgene.

In October 2014, we initiated four expansion cohorts in our ongoing phase 1 clinical trial of AG-221 in patients with IDH2 mutant-positive hematologic malignancies to assess the safety and tolerability of AG-221 at 100 mg once daily oral dose in approximately 100 patients with IDH2 mutant-positive hematologic malignancies, including AML. In the expansion cohorts, we evaluated relapsed or refractory AML patients 60 years of age and older, relapsed or refractory AML patients under age 60, untreated AML patients who decline standard of care chemotherapy and patients with other IDH2 mutant-positive advanced hematologic malignancies.

In May 2015, we announced that our ongoing phase 1 clinical trial of AG-221 had been expanded to add an additional more homogenous cohort of 125 patients with IDH2 mutant-positive AML who are in second or later relapse, are refractory to second-line induction or reinduction treatment, or have relapsed after allogeneic transplantation. Consistent with the previous expansion cohorts, AG-221 is administered at a dose of 100 mg once daily. The primary objectives of the trial are to confirm the safety and clinical activity of AG-221 in a select, highly resistant AML population. Enrollment of this cohort was completed in May 2016.

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In October 2015, Celgene, in collaboration with us, initiated IDHENTIFY, an international phase 3, multi-center, open-label, randomized clinical trial designed to compare the efficacy and safety of AG-221 versus conventional care regimens in patients 60 years or older with IDH2 mutant-positive AML that is refractory to or relapsed after second- or third-line therapy.

In December 2015, we reported additional clinical data, as of September 1, 2015, from the dose escalation phase and expansion cohorts of the ongoing phase 1 clinical trial, which was transitioned to a phase 1/2 trial in May 2015, evaluating single agent AG-221, which included 209 response-evaluable enrolled patients with IDH2 mutant-positive AML. The new data were presented at the 2015 American Society of Hematology (ASH) Annual Meeting and Exposition in Orlando, Florida and showed investigator-assessed objective responses in 79 out of 209 response-evaluable patients. Of the 79 patients who achieved an objective response, there were 37 complete remissions (CR), three complete remissions with incomplete platelet recovery (CRp), 14 marrow complete remissions (mCR), three complete remissions with incomplete hematologic recovery (CRi) and 22 partial remissions (PR). A CR is determined by using well-established criteria, which requires no evidence of leukemia in the bone marrow and blood accompanied by full restoration of all blood counts to normal ranges. A CRp means all the criteria for CR are met except that platelet counts are outside of the normal range. Platelets are one of the three major types of blood cells. A mCR means that there is no evidence for leukemia in the marrow but the blood counts have not fully restored. A CRi means there is no evidence for leukemia in the marrow but the neutrophils, a subset of white blood cells responsible for fighting bacterial infections, are outside the normal range. A partial response means all the criteria for CR are met except that the immature defective blood cells, or leukemia, in the bone marrow are in the 5% to 25% range and have been decreased by at least 50% over pretreatment. Of the 159 patients with relapsed or refractory AML, 59 achieved an objective response, including 29 CRs, one CRp, nine mCRs, three CRis and 17 PRs. Of the 24 patients with AML who declined standard of care chemotherapy, 10 achieved an objective response, including four CRs, one CRp, one mCR and four PRs. Of the 14 patients with MDS, seven achieved an objective response, including three CRs, one CRp and three mCRs. Responding relapsed or refractory AML patients were on the trial for up to 18 months with a median duration of treatment of 6.8 months, ranging from 1.8 to 18 months. Responses were durable, with median response duration of 6.9 months in patients with relapsed or refractory AML. A safety analysis was conducted for all 231 treated patients. The majority of adverse events reported by investigators were mild to moderate, with the most common being nausea, diarrhea, fatigue and febrile neutropenia. The serious adverse events, or SAEs, observed during the trial were mainly disease related. Twenty-three percent of patients had treatment-related SAEs, including notably differentiation syndrome (4 percent), leukocytosis (4 percent) and nausea (2 percent). Drug-related Grade 5 SAEs included atrial flutter (one patient), cardiac tamponade (one patient), pericardial effusion (one patient) and respiratory failure (one patient). Dose escalation has been completed and a maximum tolerated dose, or MTD, has not been reached. The first four expansion cohorts have completed enrollment. AG-221 continued to show favorable drug exposure and pharmacokinetics at all doses tested with substantial reductions in plasma levels of 2HG, which is produced by the mutated IDH2 and IDH1 proteins, to the level observed in healthy volunteers. In 2016, Celgene, in collaboration with us, intends to initiate an expansion arm of our phase 1/2 clinical trial, evaluating AG-221 in high-risk MDS patients.

Also in December 2015, we announced the initiation of a phase 1b, multicenter, international, open-label clinical trial to evaluate the safety and clinical activity of AG-221 or AG-120 in combination with induction and consolidation therapy in patients with newly diagnosed AML with an IDH2 or IDH2 mutation who are eligible for intensive chemotherapy. The trial will evaluate continuous dosing for up to one year with AG-221 administered at an initial oral dose of 100 mg once daily in patients with an IDH2 mutation or AG-120 administered at an initial oral dose of 500 mg once daily in patients with an IDH1 mutation. AG-221 or AG-120 will be administered with two types of AML induction therapies (cytarabine with either daunorubicin or idarubicin) and two types of AML consolidation therapies (mitoxantrone with etoposide [ME] or cytarabine).

In March 2016, Celgene, in collaboration with us, initiated a phase 1/2 frontline combination clinical trial, to be conducted by Celgene, of either AG-221 or AG-120 in combination with VIDAZA® (azacitidine) in newly diagnosed AML patients not eligible for intensive chemotherapy, with a phase 1 component to determine the safety of the combinations, followed by a phase 2 randomized component evaluating the safety and clinical activity of each investigational combination versus single-agent VIDAZA® using a primary endpoint of overall response rate.

In October 2014, we announced the initiation of a phase 1/2 multicenter clinical trial of AG-221 in patients with advanced solid tumors, including gliomas, as well as angioimmunoblastic T-cell lymphoma, including AITL, in each case that carry an IDH2 mutation. This phase 1/2 multicenter, open-label, dose-escalation clinical trial of AG-221, conducted in collaboration with Celgene, is designed to assess the safety, clinical activity, and tolerability of AG-221 among patients who have an IDH2 mutant-positive advanced solid tumor or AITL. The phase 1/2 clinical trial includes a dose expansion phase where three cohorts of patients with glioma, AITL and other solid tumors that are IDH2 mutant-positive are receiving AG-221 to further evaluate safety, tolerability and clinical activity in advanced solid tumors.

AG-120: lead IDH1 program

AG-120 is an orally available, selective, potent inhibitor of the mutated IDH1 protein, making it a highly targeted therapeutic candidate for the treatment of patients with cancers that harbor IDH1 mutations. Mutations in IDH1 have been identified in difficult to

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treat hematologic and solid tumor cancers, including AML, chondrosarcoma and cholangiocarcinoma where both the treatment options and prognosis for patients are poor. In March 2014, we initiated two phase 1, multicenter, open-label, dose-escalation and expansion clinical trials for AG-120, one designed to assess the safety, clinical activity and tolerability of AG-120 as a single agent in patients with advanced hematologic malignancies and the second designed to evaluate the safety, clinical activity and tolerability of AG-120 in patients with advanced solid tumors. Both trials are only enrolling patients that carry an IDH1 mutation. On May 18, 2015, we announced that the FDA granted fast track designation to AG-120 for treatment of patients with AML that harbor an IDH1 mutation. On June 10, 2015, the FDA granted us orphan drug designation for AG-120 for treatment of patients with AML.

Four expansion cohorts have been added to the ongoing phase 1 clinical trial of AG-120 in patients with advanced hematologic malignancies. These four expansion cohorts will evaluate AG-120 in 200 patients with IDH1 mutant-positive advanced hematologic malignancies. The first cohort will evaluate a more homogenous population of 125 AML patients who are in second or later relapse, are refractory to second-line induction or reinduction treatment, or have relapsed after allogeneic transplantation. The second cohort will evaluate 25 untreated AML patients. The third cohort will evaluate 25 patients with other non-AML IDH1 mutant-positive relapsed or refractory advanced hematologic malignancies. The fourth cohort will evaluate patients with relapsed IDH1 mutant-positive AML not eligible for the first arm or standard of care chemotherapy. AG-120 is administered at a 500 mg once daily oral dose, in 28-day cycles. The trial s primary objectives are to confirm the safety and clinical activity of AG-120.

In November 2015, we reported clinical data from the dose-escalation portion of our ongoing phase 1 clinical trial evaluating AG-120 in patients with IDH1 mutant-positive advanced solid tumors, including glioma, intrahepatic cholangiocarcinoma, or IHCC, and chondrosarcomas who received AG-210 administered from 200 mg to 1200 mg total daily doses. The data were presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Boston. As of the September 3, 2015 data cut-off, 62 patients had been treated with single agent AG-120, of which 55 were response-evaluable. Seven of the 11 response-evaluable patients with IDH1 mutant-positive chondrosarcoma had stable disease, with five of these patients maintaining stable disease for six months or more. One of the 20 patients with IDH1 mutant-positive IHCC had a partial response and 11 patients had stable disease, with six such patients maintaining stable disease for six months or more. Ten of the 20 patients with IDH1 mutant-positive glioma had stable disease, with four of these patients maintaining stable disease for six months or more. One of the four patients with other IDH1 mutant-positive solid tumors had stable disease. Treatment with AG-120 showed substantial reduction of 2HG in plasma and tumor tissue, and imaging results suggest that AG-120 can lower 2HG levels in the brain. AG-120 was well tolerated, with the majority of adverse events reported by investigators being mild to moderate. The most common investigator-reported adverse events were nausea, diarrhea, vomiting, anemia and QT prolongation. The majority of reported SAEs were disease related. A MTD has not been reached. We are currently enrolling four expansion cohorts of 25 patients each in (i) low grade glioma with at least six months of prior scans to assess volumetric changes, (ii) second-line cholangiocarcinoma, (iii) high grade, or metastatic, chondrosarcoma, and (iv) other solid tumors with an IDH1 mutation, who will receive the recommended dose of 500 mg of AG-120 once daily.

In December 2015, we reported new data, as of October 1, 2015, from the ongoing phase 1 clinical trial evaluating single agent AG-120, which included 87 enrolled patients with IDH1 mutant-positive advanced hematologic malignancies, of which 78 were from the dose-escalation phase and nine were from the expansion phase. The data were presented at the 2015 ASH Annual Meeting and Exposition in Orlando, Florida and showed investigator-assessed objective responses in 27 out of 78 response-evaluable patients on AG-120. Of the 27 patients who achieved an objective response, there were 12 CRs, seven CRps, six mCRs, one CRi and one PR. Patients were on the trial treatment for up to 14.1 months, with a median duration of treatment of 2.9 months, ranging from 0.1 to 14.1 months. Data continued to show durable clinical activity for AG-120, with responses maintained for up to 12.5 months and a median duration of response of 5.6 months. AG-120 continued to show favorable drug exposure and

pharmacokinetics at all doses tested and also substantially reduced plasma levels of 2HG to the level observed in healthy volunteers. The mechanism of response is consistent with differentiation, as evidenced by the maturation of the leukemic cells into infection fighting white blood cells, or neutrophils. The majority of adverse events reported by investigators were mild to moderate, with the most common being fatigue, diarrhea, pyrexia and nausea. A MTD has not been reached, and dose escalation is now complete.

As described above, in December 2015, we announced the initiation of a phase 1b, multicenter, international, open-label clinical trial of AG-221 or AG-120 in combination with induction and consolidation therapy in patients with newly diagnosed AML with an isocitrate dehydrogenase (IDH) mutation who are eligible for intensive chemotherapy. Also as described above, in the March 2016, Celgene, in collaboration with us, initiated a phase 1/2 frontline combination clinical trial, to be conducted by Celgene, of either AG-221 or AG-120 in combination with VIDAZA® (azacitidine) in newly diagnosed AML patients not eligible for intensive chemotherapy, with a phase 1 component to determine the safety of the combinations, followed by a phase 2 randomized component evaluating the safety and clinical activity of each investigational combination versus single-agent VIDAZA® using a primary endpoint of overall response rate.

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We intend to initiate a global registration-enabling phase 3 clinical trial in frontline AML patients who harbor an IDH1 mutation in the second half of 2016. In addition, we intend to initiate a randomized phase 2 clinical trial of AG-120 in patients with IDH1 mutant-positive cholangiocarcinoma in the second half of 2016.

During the three months ended March 31, 2015, Celgene exercised its exclusive option under the 2010 Agreement to license development and commercialization rights to AG-120 outside the United States. We had previously elected to exercise our option to retain development and commercialization rights to AG-120 in the United States in January 2014. Following Celgene s exercise of its exclusive option under the terms of the 2010 Agreement, Celgene leads development and commercialization outside the United States, and we lead development and commercialization in the United States. Under the 2010 Agreement, Celgene is responsible for future development and commercialization costs specific to countries outside the United States, we are responsible for future development and commercialization costs specific to the United States, and we and Celgene will equally fund the future global development costs of AG-120 that are not specific to any particular region or country. Under the 2010 Agreement, Celgene is eligible to receive tiered royalties on any net sales in the United States, and we are eligible to receive tiered royalties on any net sales outside the United States and up to $145.0 million in payments on achievement of certain milestones.

AG-881: pan-IDH program

AG-881 is an orally available, selective, brain-penetrant, pan-IDH mutant inhibitor, which provides added flexibility to our current portfolio of IDH mutant inhibitors. AG-881 successfully completed IND-enabling studies in April 2015. We and Celgene are jointly collaborating on a worldwide development program, wherein we share worldwide development costs and profits and Celgene would book any worldwide commercial sales. We will lead commercialization in the United States with both companies sharing equally in field-based commercial activities, and Celgene will lead commercialization outside of the United States with us providing one third of field-based commercial activities in the major EU markets.

We are conducting phase 1 multi-center, open-label clinical trials of AG-881, one in patients with advanced IDH1 or IDH2 mutant-positive solid tumors, including glioma, and the other in patients with advanced IDH1 or IDH2 mutant-positive hematologic malignancies whose cancer has progressed on a prior IDH inhibitor therapy. The goal of these trials is to evaluate the safety, pharmacokinetics, pharmacodynamics and clinical activity of AG-881 in advanced solid tumors and hematologic malignancies, respectively. In each trial, AG-881 will be administered continuously as a single agent dosed orally in a 28-day cycle. The first portion of each trial includes a dose-escalation phase in which cohorts of patients will receive ascending oral doses of AG-881 to determine the maximum tolerated dose and/or the recommended phase 2 dose based on safety and tolerability. The second portion of each trial is a dose expansion phase where patients will receive AG-881 to further evaluate the safety, tolerability and clinical activity of the recommended phase 2 dose.

AG-348: lead pyruvate kinase deficiency program

AG-348 is an orally available small molecule and a potent activator of the wild-type (normal) and mutated PKR enzyme, which has resulted in restoration of ATP levels and a decrease in 2,3-DPG levels in blood sampled from patients with PK deficiency in nonclinical studies. The wild-type PKR activity of AG-348 allowed the study of enzyme activation in healthy volunteers, providing an opportunity to understand the safety, dosing and pharmacodynamic activity of AG-348 prior to entering a proof-of-concept study in patients. On March 24, 2015, the FDA granted us orphan drug designation for AG-348 for treatment of patients with PK deficiency.

In April 2014, we initiated a single ascending dose, or SAD, escalation phase 1 clinical trial for AG-348 in healthy volunteers and in June 2014, we initiated a multiple ascending dose, or MAD, escalation phase 1 clinical trial for

healthy volunteers. In late 2014, we reported the SAD trial was completed and met its primary endpoint. The MAD trial completed dosing in early 2015 and has also met its primary endpoint. The primary endpoint is defined in the protocol to identify a safe and pharmacodynamically active dose and dosing schedule for AG-348 to be used in subsequent clinical studies in patients with pyruvate kinase deficiency.

In December 2014, during a poster session at ASH 2014, we reported the first clinical data from the phase 1 SAD and MAD clinical trials of AG-348 in healthy volunteers. These results provided early proof-of-mechanism for AG-348 as a novel, first-in-class, oral activator of both wild-type and mutated PKR enzymes. In these phase 1 clinical trials, dosing of AG-348 over 14-days in healthy volunteers resulted in a dose-dependent activation of the PKR pathway as evidenced by a substantial increase in ATP and decrease in 2,3-DPG levels, which are key biomarkers of PKR activity and primary indicators of PK deficiency. These data support the hypothesis that AG-348 treatment may similarly enhance PKR activity in patients with PK deficiency and thus correct the underlying defect of the disease. Results presented were from 64 healthy volunteers who received either AG-348 or placebo, which included 48 people from the completed SAD trial and 16 people in the first two cohorts of the MAD trial, which recently completed dosing. Complete safety results were reported from the SAD phase 1 clinical trial and showed that AG-348 was well tolerated. Although the MAD trial remained blinded, no serious adverse events had been reported in the first two analyzed cohorts. AG-348 also showed a favorable pharmacokinetic profile with rapid absorption, low variability and dose-proportional increase in exposure following both single and multiple doses. The observed dose-dependent changes in 2,3-DPG and ATP blood levels seen are consistent with a substantial increase in PKR enzymatic activity.

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In June 2015, we reported final clinical data from the phase 1 MAD clinical trial of AG-348 in healthy volunteers and the first data from a natural history study of PK deficiency. The data were presented at the 20th Congress of the European Hematology Association (EHA) in Vienna, Austria. Results presented were from 48 healthy volunteers who received either AG-348 or placebo for fourteen days at 15 mg, 60 mg, 120 mg, 360 mg or 700 mg twice daily or 120 mg once daily in six sequential cohorts. The study showed that AG-348 was well tolerated, with most adverse events occurring in the highest dose group (700 mg), with all but one being mild to moderate. Thirty-two of 36 healthy volunteers receiving AG-348 completed the study. Two volunteers receiving AG-348 withdrew due to adverse events, including drug eruption (60 mg) and Grade 3 liver function test abnormalities (700 mg), which resolved after treatment discontinuation. Two additional AG-348 volunteers (both 700 mg) withdrew consent due to nausea or vomiting. Serum hormone changes consistent with reversible aromatase inhibition were observed. AG-348 also showed a favorable pharmacokinetic profile with rapid absorption, low to moderate variability and a dose-proportional increase in exposure following multiple doses.

As predicted by the mechanism of action of AG-348, there was a robust activation of pyruvate kinase as evidenced by a decrease in 2,3-DPG (2,3-diphosphoglycerate) and increase in ATP (adenosine triphosphate) in blood of healthy volunteers. The decrease in 2,3-DPG was approximately 50 percent for doses 120 mg and higher with levels returning back to baseline approximately 72 hours after AG-348 was discontinued. There was also an approximately 50 percent increase in ATP in blood with AG-348 at doses 60 mg and higher in healthy volunteers.

In June 2015, we initiated DRIVE PK, a global phase 2, first-in-patient, open-label safety and efficacy clinical trial of AG-348 in adult, transfusion-independent patients with PK deficiency. The multi-center, randomized trial will include two arms with 25 patients each. The patients in the first arm will receive 50 mg twice daily, and the patients in the second arm will receive 300 mg twice daily. The trial will include a six-month dosing period with the opportunity for continued treatment beyond six months based on safety and clinical activity. In July 2015, we dosed the first-patient in this phase 2 clinical trial, and we expect to present the first data from this trial in June 2016 at the 21st Congress of EHA in Copenhagen, Denmark.

We have worldwide development and commercial rights to AG-348 and expect to fund the future development and commercialization costs related to this program.

AG-519: a second novel PKR activator

AG-519 is an orally available small molecule and our second product candidate that is a potent activator of the PKR enzyme. We initiated a placebo-controlled phase 1 clinical trial of AG-519 in healthy volunteers in the first quarter of 2016. This trial is an integrated single ascending dose and multiple ascending dose trial. We expect to present the first data from this trial in June 2016 at the 21st Congress of EHA in Copenhagen, Denmark.

We have worldwide development and commercial rights to AG-519 and expect to fund the future development and commercialization costs related to this program.

Other research and platform programs

Other research and platform programs include activities related to exploratory efforts, target validation and lead optimization for our discovery and follow-on programs and our proprietary metabolomics platform.

We use our employee and infrastructure resources across multiple research and development programs, and we allocate internal employee-related and infrastructure costs, as well as certain third-party costs, net of reimbursements from Celgene, to each of these programs based on the personnel resources allocated to such program. Our research

and development expenses, by major program, are outlined in the table below:

(in thousands)	Three Months Ended March 31, 2016	2015
IDH2 (AG-221)	$ 2,198	$ 3,329
IDH1 (AG-120)	13,127	10,417
Pan IDH (AG-881)	3,002	3,873
PK deficiency (AG-348)	5,092	5,071
PKR activator (AG-519)	4,805	613
Other research and platform programs	15,814	9,140
Total research and development expenses	$ 44,038	$ 32,443

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Research and development expenses for AG-221 for the three months ended March 31, 2016 and 2015 are net of $0.5 million and $4.4 million, respectively, in reimbursement of certain third-party costs under the 2010 Agreement, as amended, which are classified as a reduction of research and development expense.

Research and development expenses for AG-120 for the three months ended March 31, 2016 are net of $6.6 million in reimbursement of certain third-party and internal costs under the 2010 Agreement, as amended, which are classified as a reduction of research and development expense. No reimbursements were recognized in our research and development costs during the three months ended March 31, 2015.

Research and development expenses for AG-881 for the three months ended March 31, 2016 are net of $1.7 million in reimbursement of certain third-party and internal costs under the AG-881 Agreements, which are classified as a reduction of research and development expense. No reimbursements were recognized in our research and development costs during the three months ended March 31, 2015.

The successful development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from AG-221, AG-120, AG-881, AG-348, AG-519 or any of our other product candidates. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

- establishing an appropriate safety profile with IND and/or NDA enabling toxicology studies;
- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others; and
- maintaining an acceptable safety profile of the products following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily

due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our product candidate development programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, business development, legal and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

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We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities and potential commercialization of our product candidates. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses.

Critical Accounting Policies and Estimates

Our critical accounting policies are those policies which require the most significant judgments and estimates in the preparation of our consolidated financial statements. Management has determined that our most critical accounting policies are those relating to revenue recognition, accrued research and development expenses and stock-based compensation. There have been no significant changes to our critical accounting policies discussed in the Annual Report on Form 10-K for the year ended December 31, 2015.

Results of Operations

Comparison of three months ended March 31, 2016 and 2015

The following table summarizes our results of operations for the three months ended March 31, 2016 and 2015, together with the changes in those items in dollars and as a percentage:

	Three Months Ended March 31,			
(in thousands)	**2016**	**2015**	**Dollar Change**	**% Change**
Collaboration revenue related party	$ 31,281	$ 34,202	$ (2,921)	(9)%
Operating expenses:				
Research and development (net of $8,794 and $4,366 of cost reimbursement from related party for the three months ended March 31, 2016 and 2015)	44,038	32,443	11,595	36
General and administrative	10,837	6,954	3,883	56
Loss from operations	(23,594)	(5,195)	(18,399)	354
Interest income	396	238	158	66
Net loss	$ (23,198)	$ (4,957)	$ (18,241)	368%

Revenue. For the three months ended March 31, 2016, we recognized $31.3 million in revenue, which includes a $25 million milestone payment related to a substantive clinical development milestone achieved. The remaining $6.3 million in revenue was recognized under the current revenue recognition accounting guidance.

For the three months ended March 31, 2015, we recognized $34.2 million in revenue, which includes the recognition of $15.8 million related to the delivery of an ex. U.S. license for AG-120. During the same period we recognized an additional $5.1 million of revenue due to a change in estimate related to transitioning primary development responsibilities of AG-221 to Celgene for later stage development, at which point Celgene would became the lead development party for AG-221. Including the $3.8 million presented as a reduction of research and development expenditures, the net change reduced our net loss by $8.9 million. The remaining $13.3 million in revenue was recognized under the current revenue recognition accounting guidance.

Research and Development Expense. The increase in research and development expenses was primarily attributable to net increases of $1.5 million in external services and $10.1 million in internal expenses; both of these increases are inclusive of $8.8 million in reimbursement of certain costs related to AG-221, AG-120 and AG-881, which are recorded as a reduction of research and development expenses. During the three months ended March 31, 2016 and 2015, we recognized certain cost reimbursements related to our on-going development activities under our IDH programs for which we are no longer acting as the principal in the transaction as a reduction of research and development expenses.

The increase in external services in 2016 was attributable to the following:

decreases of approximately $1.0 million, $2.2 million, $1.0 million and $1.3 million for external clinical studies and manufacturing activities for our lead product candidates AG-221, AG-120, AG-348 and AG-881, respectively;

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an increase of approximately $2.7 million for preclinical studies for our product candidate AG-519; and

an increase of approximately $4.3 million for costs related to other early research and platform programs.

We incurred approximately $10.1 million of additional internal research and development expenses related to the following:

an increase of $7.4 million in personnel costs related to an increase in our internal headcount of 52%, which includes an increase of $2.9 million in stock-based compensation expense; and

an increase of approximately $2.7 million for facilities and other related expenses.

General and Administrative Expense. The increase in general and administrative expenses was primarily attributable to the following:

an increase of $2.8 million in personnel costs related to an increase in our internal headcount of 47% which includes an increase of $1.1 million for stock-based compensation expense;

an increase of $0.3 million in professional service costs and insurance costs; and

an increase of $0.8 million in certain operating expenses, including consulting and facility costs.

Interest Income. The increase is attributable to a more diversified investment portfolio, resulting in higher interest earned on investments.

Provision for Income Tax. We did not have a provision for income taxes during the three months ended March 31, 2016 or 2015 due to our net loss.

Liquidity and Capital Resources

Sources of liquidity

Since our inception, and through March 31, 2016, we have funded our operations through upfront, extension and cost reimbursement payments related to our collaboration agreements with Celgene, proceeds received from our issuance of preferred stock, our IPO and our follow-on public offerings, including private placement of common stock to an affiliate of Celgene, which was completed concurrently with our IPO.

In addition to our existing cash, cash equivalents and marketable securities, we are eligible to earn a significant amount of milestone payments and are entitled to cost reimbursements under our collaboration agreements with Celgene. Our ability to earn the milestone payments and cost reimbursements and the timing of earning these amounts are dependent upon the timing and outcome of our development, regulatory and commercial activities and are uncertain at this time. Our right to payments under our collaboration agreements is our only committed potential external source of funds.

Cash flows

The following table provides information regarding our cash flows for the three months ended March 31, 2016 and 2015:

	Three Months Ended, March 31,	
(in thousands)	**2016**	**2015**
Net cash used in operating activities	$ (19,009)	$ (25,585)
Net cash (used in) provided by investing activities	(14,828)	44,988
Net cash provided by financing activities	1,108	1,822
Net (decrease) increase in cash and cash equivalents	$ (32,729)	$ 21,225

Net cash used in operating activities. The use of cash in all periods resulted primarily from funding our net losses adjusted for non-cash charges and changes in components of working capital. The net loss was primarily attributable to increased operating expenses which relates to increases in clinical study costs due to advancements in our lead product candidates, expanded facilities and increased staffing needs due to our expanding operations offset by amounts reimbursed by Celgene. During the three months ended March 31, 2016, we received $35.1 million related to our collaboration agreements, including a $25.0 million milestone payment in conjunction with the achievement of a substantive development milestone, and $2.8 million as reimbursement of tenant improvements compared to $6.6 million received related to our collaboration agreements during the three months ended March 31, 2015. We received $3.8 million of refundable income taxes during the three months ended March 31, 2015, related to a previously filed carryback claim.

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Net cash (used in) provided by investing activities. The cash used in investing activities for the three months ended March 31, 2016 was primarily the result of lower proceeds from maturities and sales of marketable securities in comparison to purchases of marketable securities. In addition we incurred $2.5 million in purchases of property and equipment. The cash provided by investing activities for the three months ended March 31, 2015 was primarily the result of higher proceeds from maturities and sales of marketable securities, in comparison to purchases of marketable securities, offset by $3.8 million in purchases of property and equipment.

Net cash provided by financing activities. The cash provided by financing activities for the three months ended March 31, 2016 and 2015 was the result of proceeds received from stock option exercises and proceeds received from stock purchases made pursuant to our employee stock purchase plan.

Funding requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research, development and clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of Celgene or other collaborators. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We expect that our existing cash, cash equivalents and marketable securities as of March 31, 2016, together with anticipated interest income, and anticipated expense reimbursements under our collaboration agreements with Celgene will enable us to fund our operating expenses and capital expenditure requirements until at least late 2017. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the success of our collaborations with Celgene;
- the extent to which we acquire or in-license other medicines and technologies;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- our ability to establish and maintain additional collaborations on favorable terms, if at all.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenue, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaborations with Celgene. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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Off-balance Sheet Arrangements

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable Securities and Exchange Commission rules.

Contractual obligations

During the three months ended March 31, 2016, we entered into agreements in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes. These contractual obligations are cancelable at any time by us, generally upon 30 days prior written notice to the vendor. Under these agreements, as of March 31, 2016 we are obligated to pay up to $55.3 million to these vendors.

During the three months ended March 31, 2016, there were no other material changes to our contractual obligations and commitments described under Management s Discussion and Analysis of Financial Condition and Results of Operations in the Annual Report on Form 10-K for the year ended December 31, 2015.

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Item 3. Quantitative and Qualitative Disclosures About Market Risk.

We are exposed to market risk related to changes in interest rates. As of March 31, 2016 and December 31, 2015, we had cash, cash equivalents and marketable securities of $355.8 million and $375.9 million, respectively, consisting primarily of investments in U.S. Treasuries and certificates of deposit. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term marketable securities. Our marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we do not believe an immediate 10% change in interest rates would have a material effect on the fair market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

We are also exposed to market risk related to changes in foreign currency exchange rates. We have contracts with CROs that are located in Asia and Europe that are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk. As of March 31, 2016 and December 31, 2015, we had minimal or no liabilities denominated in foreign currencies.

Item 4. Controls and Procedures.

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures. Based on that evaluation of our disclosure controls and procedures as of March 31, 2016, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act are recorded, processed, summarized and reported within the time periods specified in the SEC s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

No change in our internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, occurred during the fiscal quarter ended March 31, 2016 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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PART II. OTHER INFORMATION

Item 1A. Risk Factors

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained herein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. The words anticipate, believe, estimate, expect, intend, may, plan, predict, potential, will, would, could, should, continue and similar expressions are intended to identify forward-lookin statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. You should read this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from what we expect. The risks described are not the only risks facing our company. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition and/or operating results. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. These risk factors restate and supersede the risk factors set forth under the heading Risk Factors in our Annual Report on Form 10-K for the year ended December 31, 2015.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net losses were $117.7 million, $53.5 million and $39.4 million for the years ended December 31, 2015, 2014 and 2013, respectively, and $23.2 million for the three months ended March 31, 2016. As of March 31, 2016, we had an accumulated deficit of $307.9 million. We have never generated any revenue from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations primarily through private placements of our preferred stock, our initial public offering and the concurrent private placement, our follow-on public offerings and our collaboration agreements with Celgene Corporate, or Celgene, focused on cancer metabolism. We have devoted substantially all of our efforts to research and development. We are in clinical development stages of our product candidates and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. Although we may from time to time report profitable results, we expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- continue our research and preclinical development of our product candidates;

seek to identify additional product candidates;

initiate and continue clinical trials for our product candidates, including our lead product candidates AG-221, AG-120, AG-881 and AG-348;

seek marketing approvals for our product candidates that successfully complete clinical trials;

ultimately establish a sales, marketing and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval;

require the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization;

maintain, expand and protect our intellectual property portfolio;

hire additional clinical, quality control and scientific personnel;

add additional personnel to support our product development and planned future commercialization efforts and our operations;

add equipment and physical infrastructure to support our research and development; and

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acquire or in-license other medicines and technologies.

To become and remain profitable, we must develop and eventually commercialize a medicine or medicines with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those medicines for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenue that are significant or large enough to achieve profitability. We are currently in clinical testing stages for our lead product candidates. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate and continue clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of Celgene or other collaborators. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We expect that our existing cash, cash equivalents and marketable securities as of March 31, 2016, together with anticipated interest income, and the anticipated expense reimbursements under our collaboration agreements with Celgene will fund our operating and capital expenditure requirements until at least late 2017. Our estimate as to how long we expect our existing cash and cash equivalents, to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future capital requirements will depend on many factors, including:

the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;

the success of, and developments regarding, our collaborations with Celgene;

the costs, timing and outcome of regulatory review of our product candidates;

the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;

our ability to establish and maintain additional collaborations on favorable terms, if at all; and

the extent to which we acquire or in-license other medicines and technologies.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenue, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaborations with Celgene, which are limited in scope and duration. For example, the discovery phase under our 2010 collaboration agreement with Celgene, or 2010 Agreement, expired in April 2016 and we will no longer receive payments from Celgene with respect to extensions of the discovery phase under the 2010 Agreement. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that

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include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management s ability to oversee the development of our product candidates.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage company. We were founded in the second half of 2007 and commenced operations in late 2008. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our technology, identifying potential product candidates and undertaking preclinical and clinical studies of our product candidates. All of our product candidates are still in preclinical and clinical development. We have not yet demonstrated our ability to successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop one new medicine from the time it is discovered to when it is available for treating patients, assuming that it successfully completes all stages of research and development and achieves marketing approval, all of which is highly uncertain. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Risks Related to the Discovery, Development, and Commercialization of our Product Candidates

We do not know whether we will be able to develop any medicines of commercial value, based on our approach to the discovery and development of product candidates that target cellular metabolism.

Our scientific approach focuses on using our proprietary technology to identify key metabolic enzymes in cancer, RGDs or other diseased cells in the laboratory and then using these key enzymes to screen for and identify product candidates targeting cellular metabolism.

Any medicines that we develop may not effectively correct metabolic pathways. Even if we are able to develop a product candidate that targets cellular metabolism in preclinical studies, we may not succeed in demonstrating safety and efficacy of the product candidate in human clinical trials. Our focus on using our proprietary technology to screen for and identify product candidates targeting cellular metabolism may not result in the discovery and development of commercially viable medicines to treat cancer or RGDs.

We may not be successful in our efforts to identify or discover potential product candidates.

A key element of our strategy is to identify and test compounds that target cellular metabolism in a variety of different types of cancer and RGDs. A significant portion of the research that we are conducting involves new compounds and drug discovery methods, including our proprietary technology. The drug discovery that we are conducting using our proprietary technology may not be successful in identifying compounds that are useful in treating cancer or RGDs. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying appropriate biomarkers or potential product candidates; or

- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

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Research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful.

If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

We depend heavily on the success of our most advanced product candidates. All of our lead product candidates are still in clinical development. Clinical trials of our product candidates may not be successful. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification of our lead product candidates, AG-221, AG-120 and AG-881 for the treatment of hematological and solid tumors and AG-348 for the treatment of PK deficiency. We or our collaborator have initiated clinical trials for our lead product candidates. We have not commenced clinical trials for any of our other product candidates. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of these product candidates by our collaborators and us. The success of our product candidates will depend on many factors, including the following:

- successful enrollment in, and completion of, clinical trials;
- safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority for marketing approval
- timely receipt of marketing approvals from applicable regulatory authorities;
- establishing both clinical and commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- the performance of our collaborators;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our medicines;
- launching commercial sales of the medicines, if and when approved, whether alone or in collaboration with others;

acceptance of the medicines, if and when approved, by patients, the medical community and third-party payors;

effectively competing with other therapies;

continuing acceptable safety profile for the medicines following approval;

enforcing and defending intellectual property rights and claims; and

achieving desirable medicinal properties for the intended indications.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborator. If we or our collaborators do not achieve one or more of these factors in a timely manner or at all, we or our collaborators could experience significant delays or an inability to successfully commercialize our most advanced product candidates, which would materially harm our business.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We, and any collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the European Medicines Agency, or the EMA, impose similar requirements. We have not previously submitted a new drug application, or NDA, to the FDA or similar drug approval filings to comparable foreign regulatory authorities for any of our product candidates. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable.

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It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any future collaborators, and impair our ability to generate revenue from product sales, regulatory and commercialization milestones and royalties. Moreover, if we or our collaborators are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we or our collaborators are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we or our collaborators may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the medicine removed from the market after obtaining marketing approval.

Our failure to successfully complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business.

If we, or any collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our product candidates, potential clinical development, marketing approval or commercialization of our product candidates could be delayed or prevented.

We or our collaborators may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

regulators or institutional review boards may not authorize us, our collaborators or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

we or our collaborators may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

clinical trials of our product candidates may produce negative or inconclusive results, and we or our collaborators may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;

the number of patients required for clinical trials of our product candidates may be larger than we anticipate; enrollment in these clinical trials, which may be particularly challenging for some of the orphan diseases we target in our RGD programs, may be slower than we anticipate; or participants may drop out of these clinical trials at a higher rate than we anticipate;

third-party contractors used by us or our collaborators may fail to comply with regulatory requirements or meet their contractual obligations in a timely manner, or at all;

we or our collaborators might have to suspend or terminate clinical trials of our product candidates for various reasons, including a fin