

AGIOS PHARMACEUTICALS INC

Form 10-Q

May 09, 2016

Table of Contents

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 10-Q

(Mark One)

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

For the quarterly period ended 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 (State or Other Jurisdiction of	26-0662915 (I.R.S. Employer
Incorporation or Organization)	Identification No.)
88 Sidney Street, Cambridge, Massachusetts (Address of Principal Executive Offices)	02139 (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 No

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 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

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

Table of Contents

AGIOS PHARMACEUTICALS, INC.

FORM 10-Q

FOR THE QUARTERLY PERIOD ENDED MARCH 31, 2016

TABLE OF CONTENTS

	Page No.
<u>PART I. FINANCIAL INFORMATION</u>	3
Item 1. <u>Financial Statements (Unaudited)</u>	3
<u>Condensed Consolidated Balance Sheets as of March 31, 2016 and December 31, 2015</u>	3
<u>Condensed Consolidated Statements of Operations for the Three Months Ended March 31, 2016 and 2015</u>	4
<u>Condensed Consolidated Statements of Comprehensive Loss for the Three Months Ended March 31, 2016 and 2015</u>	5
<u>Condensed Consolidated Statements of Cash Flows for the Three Months Ended March 31, 2016 and 2015</u>	6
<u>Notes to Condensed Consolidated Financial Statements</u>	7
Item 2. <u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	19
Item 3. <u>Quantitative and Qualitative Disclosures About Market Risk</u>	31
Item 4. <u>Controls and Procedures</u>	31
<u>PART II. OTHER INFORMATION</u>	32
Item 1A. <u>Risk Factors</u>	32
Item 6. <u>Exhibits</u>	58
<u>Signatures</u>	59

Table of Contents**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

Edgar Filing: AGIOS PHARMACEUTICALS INC - Form 10-Q

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.

Table of Contents**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.

Table of Contents**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.

Table of Contents**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.

Table of Contents

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.

Table of Contents

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):

Table of Contents

	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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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

Table of Contents

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

Table of Contents

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-

Table of Contents

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

Table of Contents*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 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

Table of Contents

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

Edgar Filing: AGIOS PHARMACEUTICALS INC - Form 10-Q

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

Table of Contents**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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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 IDH1 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

Table of Contents

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-120 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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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:

(in thousands)	Three Months Ended		Dollar Change	% Change
	2016	2015		
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 become 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;

Table of Contents

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:

(in thousands)	Three Months Ended, March 31,	
	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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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-looking 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

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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 finding that the participants are being exposed to unacceptable health risks;

regulators, institutional review boards, or the data safety monitoring board for such trials may require that we, our collaborators or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

the cost of clinical trials of our product candidates may be greater than anticipated;

the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and

our product candidates may have undesirable side effects or other unexpected characteristics, causing us, our collaborators or our investigators, regulators or institutional review boards to suspend or terminate the trials.

Table of Contents

Product development costs for us, or any collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we, or any future collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of any collaborators, to bring products to market before we, or any collaborators, do and impair our ability, or the ability of any collaborators, to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We or our collaborators may not be able to initiate or continue clinical trials for our product candidates if we or they are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States. Enrollment may be particularly challenging for some of the orphan diseases we target in our RGD programs. In addition, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors including:

severity of the disease under investigation;

availability and efficacy of approved medications for the disease under investigation;

eligibility criteria for the study in question;

perceived risks and benefits of the product candidate under study;

efforts to facilitate timely enrollment in clinical trials;

patient referral practices of physicians;

the ability to monitor patients adequately during and after treatment; and

proximity and availability of clinical trial sites for prospective patients.

Utilizing our precision medicine approach, we focus our development activities on genetically or biomarker defined patients most likely to respond to our therapies. As a result, the potential patient populations for our clinical trials are narrowed, and we may experience difficulties in identifying and enrolling a sufficient number of patients in our clinical trials. In particular, the successful completion of our clinical development programs for AG-348 and AG-519 for the treatment of PK deficiency is dependent upon our ability to enroll a sufficient number of patients with PK deficiency. PK deficiency is a rare disease with a small patient population. Further, there are only a limited number of specialist physicians that regularly treat patients with PK deficiency and major clinical centers that support PK deficiency are concentrated in a few geographic regions. The small population of patients, the nature of the disease and limited trial sites may make it difficult for us to enroll enough patients to complete our clinical trials for AG-348 and AG-519 for PK deficiency in a timely and cost-effective manner.

In addition, other companies are conducting clinical trials, or may in the future conduct clinical trials, which may have similar eligibility criteria as our current or future clinical trials. For example, Novartis International AG, or Novartis, is currently conducting a phase 1 clinical trial of its IDH1 mutant inhibitor, IDH305, in patients with advanced malignancies, and this trial may compete with our clinical trials of AG-120 and/or AG-881 for eligible patients with hematological and/or other malignancies harboring an IDH1 mutation. Competition for these patients may make it difficult for us to enroll enough patients to complete our clinical trials for AG-120 or AG-881 in a timely and cost-effective manner.

Furthermore, we rely on contract research organizations, or CROs, and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance. Our or our collaborators inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Table of Contents

If serious adverse side effects or unexpected characteristics are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.

All of our lead product candidates are still in clinical stage development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. Adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, any future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label, or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If adverse effects were to arise in patients being treated with any of our product candidates, it could require us to halt, delay or interrupt clinical trials of such product candidate or adversely affect our ability to obtain requisite approvals to advance the development and commercialization of such product candidate. If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any future collaborators, may need to abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in earlier stage testing for treating cancer, RGDs or other diseases have later been found to cause side effects that prevented further development of the compound.

Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or future collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other

product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial medicines or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Under the 2010 Agreement, we have the right, exercisable during a specified period following FDA acceptance of the applicable investigational new drug application, or IND, to convert one of every three co-commercialized licensed programs into a split licensed program, for which we retain the United States rights. Due to the limited exercise period, we may have to choose whether a co-commercialized program will be a split licensed program before we have as much information as we would like on another co-commercialized program, including whether and when such co-commercialized program may receive FDA acceptance of the applicable IND. Our IDH2 program is not a split licensed program. We have chosen AG-120, and our IDH1 program, as our first split licensed program under the 2010 Agreement. As a result of such incomplete information or due to incorrect analysis by us, we may select a split licensed program that later proves to have less commercial potential than an alternative or none at all.

Table of Contents

If we are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our therapeutics.

Because we are focused on precision medicine, in which predictive biomarkers will be used to identify the right patients for our drug candidates, we believe that our success may depend, in part, on our ability to develop companion diagnostics, which are assays or tests to identify an appropriate patient population for these drug candidates. There has been limited success to date industry-wide in developing these types of companion diagnostics. To be successful, we need to address a number of scientific, technical and logistical challenges. We have little experience in the development of diagnostics and may not be successful in developing appropriate diagnostics to pair with any of our therapeutic product candidates that receive marketing approval. Companion diagnostics are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory approval prior to commercialization. Given our limited experience in developing diagnostics, we rely and expect to continue to rely in part or in whole on third parties for their design and manufacture. We also depend on Celgene for the development of diagnostics for some of our cancer therapeutic product candidates. If any parties, including without limitation Celgene or us, or any third parties engaged by Celgene or us are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience delays in doing so:

the development of our therapeutic product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;

our therapeutic product candidates may not receive marketing approval if safe and effective use of a therapeutic product candidate depends on an in vitro diagnostic; and

we may not realize the full commercial potential of any therapeutics that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from therapy with our medicines.

As a result, our business would be harmed, possibly materially.

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates.

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any NDAs that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. If the FDA does not accept or approve our NDAs for any of our product candidates, it may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA-required trials or studies, approval of any NDA or application that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates, generating revenue and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

Even if any of our product candidates receives marketing approval, we or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any future collaborators, to market the product.

Clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

regulatory authorities may withdraw their approval of the product or seize the product;

we, or any future collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;

additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;

we may be subject to fines, injunctions or the imposition of civil or criminal penalties;

regulatory authorities may require the addition of labeling statements, such as a black box warning or a contraindication;

Table of Contents

we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;

we, or any future collaborators, could be sued and held liable for harm caused to patients;

the product may become less competitive; and

our reputation may suffer.

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

efficacy and potential advantages compared to alternative treatments;

the approval, availability, market acceptance and reimbursement for the companion diagnostic;

the ability to offer our medicines for sale at competitive prices;

convenience and ease of administration compared to alternative treatments;

the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;

ensuring uninterrupted product supply;

the strength of marketing and distribution support;

sufficient third-party coverage or reimbursement; and

the prevalence and severity of any side effects.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have little experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved medicine for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to other third parties. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our medicines on our own include:

our inability to recruit and retain adequate numbers of effective sales and marketing personnel;

the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;

the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

unforeseen costs and expenses associated with creating an independent sales and marketing organization. If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability of product revenue to us are likely to be lower than if we were to market and sell any medicines that we develop

Table of Contents

ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our medicines effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and we and our collaborators will face competition with respect to any product candidates that we or they may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates, such as acute myelogenous leukemia and high risk myelodysplasia. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches, for example, in the area of RGDs. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are developing most of our initial product candidates for the treatment of cancer. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy, and cancer drugs are frequently prescribed off-label by healthcare professionals. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates.

We are also pursuing product candidates to treat patients with RGDs. There are a variety of treatment options available, including a number of marketed enzyme replacement therapies, for treating patients with RGDs. In addition to currently marketed therapies, there are also a number of products that are either enzyme replacement therapies or gene therapies in various stages of clinical development to treat RGDs. These products in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain marketing approval.

There are also a number of product candidates in preclinical or clinical development by third parties to treat cancer and RGDs by targeting cellular metabolism. These companies include large pharmaceutical companies, including AstraZeneca plc, Eli Lilly and Company, Roche Holdings Inc. and its subsidiary Genentech, Inc., GlaxoSmithKline plc, Merck & Co., Novartis with its IDH1 mutant inhibitor IDH305, Pfizer, Inc., and Genzyme, a Sanofi company. There are also biotechnology companies of various sizes that are developing therapies to target cellular metabolism, including Alexion Pharmaceuticals, Inc., BioMarin Pharmaceutical Inc., Calithera Biosciences, Inc., Cornerstone Pharmaceuticals, Inc., Forma Therapeutics Holdings LLC, Shire Biochem Inc., Raze Therapeutics, Inc. and Selvita S.A. Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. In addition, our

competitors may discover biomarkers that more efficiently measure metabolic pathways than our methods, which may give them a competitive advantage in developing potential products. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other clinical stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Table of Contents

Even if we or our collaborators are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, we, or any future collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize any of our product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenue. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be

incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for any product candidate that we, or any future collaborator, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Table of Contents

Product liability lawsuits against us or our collaborators could cause us or our collaborators to incur substantial liabilities and could limit commercialization of any medicines that we or they may develop.

We and our collaborators face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we or they commercially sell any medicines that we or they may develop. If we or our collaborators cannot successfully defend ourselves or themselves against claims that our product candidates or medicines caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

decreased demand for any product candidates or medicines that we may develop;

injury to our reputation and significant negative media attention;

withdrawal of clinical trial participants;

significant costs to defend the related litigation;

substantial monetary awards to trial participants or patients;

loss of revenue;

reduced resources of our management to pursue our business strategy; and

the inability to commercialize any medicines that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we continue clinical trials and if we successfully commercialize any medicine. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. In addition, if one of our collaboration partners were to become subject to product liability claims or were unable to successfully defend themselves against such claims, any such collaboration partner could be more likely to terminate such relationship with us and therefore substantially limit the commercial potential of our products.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the

disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

We rely significantly on information technology and any failure, inadequacy, interruption or security lapse of that technology, including any cyber security incidents, could harm our ability to operate our business effectively.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our product research, development and commercialization efforts could be delayed.

Table of Contents

Risks Related to Our Dependence on Third Parties

We depend on our collaborations with Celgene and may depend on collaborations with additional third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

In April 2010, we entered into the 2010 Agreement. The collaboration involves a complex allocation of rights, provides for milestone payments to us based on the achievement of specified clinical development, regulatory and commercial milestones, provides us with royalty-based revenue if certain product candidates are successfully commercialized and provides for cost reimbursements of certain development activities. The discovery phase under the 2010 Agreement concluded in April 2016 and we will no longer receive additional payments to extend the term of the discovery phase. In April 2015, we entered into the AG-881 Agreements. We cannot predict the success of these collaborations.

We may seek other third-party collaborators for the development and commercialization of our product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates, including our collaborations with Celgene, pose the following risks to us:

Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations. For example, under our collaborations with Celgene, development and commercialization plans and strategies for licensed programs, such as AG-221, will be conducted in accordance with a plan and budget approved by a joint committee comprised of equal numbers of representatives from each of us and Celgene, as to which Celgene may have final decision-making authority.

Collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities. For example, under the 2010 Agreement, it is possible for Celgene to elect not to progress into preclinical development a product candidate that we have nominated and the joint research committee confirmed, without triggering a termination of the collaboration arrangement.

Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing, which may result in a need for additional capital to pursue further development or commercialization of the applicable product candidate. For example, under the 2010 Agreement, it is possible for Celgene to terminate the agreement, upon 90 days prior written notice, with respect to any product candidate at any point in the research, development and clinical trial process,

without triggering a termination of the remainder of the collaboration arrangement.

Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our medicines or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.

Collaborators with marketing and distribution rights to one or more medicines may not commit sufficient resources to the marketing and distribution of such medicine or medicines.

Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, under specified circumstances Celgene has the first right to maintain or defend our intellectual property rights under the 2010 Agreement with respect to certain licensed programs and, although we may have the right to assume the maintenance and defense of our intellectual property rights if Celgene does not, our ability to do so may be compromised by Celgene's actions.

Disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our medicines or product candidates or that result in costly litigation or arbitration that diverts management attention and resources.

Table of Contents

We may lose certain valuable rights under circumstances identified in our collaborations, including, in the case of our agreements with Celgene, if we undergo a change of control.

Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates. For example, Celgene can terminate its agreements with us, in their entirety or with respect to any program under the 2010 Agreement, upon 90 days' notice and can terminate each entire agreement with us in connection with a material breach of the agreement by us that remains uncured for 60 days.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

We may seek to establish additional collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such collaboration could be more attractive than the one with us for our product candidate.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. For example, during the discovery phase of the 2010 Agreement, we may not directly or indirectly develop, manufacture or commercialize, except pursuant to the agreement, any medicine or product candidate for any cancer indication: with specified activity against certain metabolic targets except in connection with certain third-party collaborations; or with specified activity against any collaboration target, or any target for which Celgene is conducting an independent program that we elected not to buy in to. Following the discovery phase until termination or expiration of the 2010 Agreement, either in its entirety or with respect to the relevant program, we may not directly or indirectly develop, manufacture or commercialize, outside of the collaboration, any medicine or product candidate with specified activity against any collaboration target that is within a licensed program or against any former collaboration target against which Celgene is conducting an independent

program under the agreement.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Table of Contents

We rely and expect to continue to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We do not independently conduct clinical trials of any of our product candidates. We rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. In addition we currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third-parties or to do so on commercially reasonable terms. Switching or adding additional third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays may occur in our product development activities. Although we seek to carefully manage our relationships with our CROs, we could encounter similar challenges or delays in the future and these challenges or delays could have a material adverse impact on our business, financial condition and prospects.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with current good clinical practices, or cGCP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these cGCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the European Medicines Agency, or EMA, or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with cGCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices, or cGMP, regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, clinicaltrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. In addition, these third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our on-going clinical, nonclinical and preclinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines. As a result, our results of operations and the commercial prospects for our medicines would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We also rely and expect to continue to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for late-stage clinical trials and for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or medicines or that such supply will not be available to us at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing and for commercial supply of any of these product candidates for which we or our collaborators obtain marketing approval. To date, we have obtained materials for AG-221, AG-120, AG-881, AG-348 and AG-519 for our ongoing preclinical and clinical testing from third-party manufacturers. We do not have any long-term supply agreements with the third-party manufacturers, and we purchase our required drug supply on a purchase order basis.

Table of Contents

We may be unable to establish any long-term supply agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

reliance on the third party for regulatory compliance and quality assurance;

the possible breach of the manufacturing agreement by the third party;

the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and

reliance on the third party for regulatory compliance, quality assurance, environmental and safety and pharmacovigilance reporting.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements on a global basis. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations.

Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for bulk drug substances. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent or trade secret protection for our medicines and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize medicines and technology similar or identical to ours, and our ability to successfully commercialize our medicines and technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary medicines and technology. We seek to protect our proprietary position by

filing patent applications in the United States and abroad related to our novel technologies and medicines that are important to our business. We do not yet have issued patents for all our lead product candidates in all markets we intend to commercialize.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

We may in the future license patent rights that are valuable to our business from third parties, in which event we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or medicines underlying such licenses. We cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties also apply to patent rights we own.

Table of Contents

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or medicines or that effectively prevent others from commercializing competitive technologies and medicines. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore we cannot be certain that we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, prior to March 2013, in the United States, the first to make the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. Beginning in March 2013, the United States transitioned to a first inventor to file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent. We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize medicines without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and medicines. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by

disclosure during this type of litigation.

Third parties may initiate legal proceedings alleging that we or our collaborators are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. We have in the past and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our medicines and technology, including interference proceedings before the U.S. Patent and Trademark Office. For example, in 2011, The Leonard and Madlyn Abramson Family Cancer Research Institute at the Abramson Cancer Center of the University of Pennsylvania initiated a lawsuit against us, one of our founders, Craig B. Thompson, M.D., and Celgene, alleging misappropriation of intellectual property and, in 2012, the Trustees of the University of Pennsylvania initiated a similar lawsuit against us and Dr. Thompson. Each of these lawsuits was settled in 2012. No other legal proceedings have been filed against us to date. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we or one of our collaborators are found to infringe a third party's intellectual property

Table of Contents

rights, we or they could be required to obtain a license from such third party to continue developing and marketing our medicines and technology. However, we or our collaborators may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or our collaborators were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us. We or our collaborators could be forced, including by court order, to cease developing and commercializing the infringing technology or medicine. In addition, we or our collaborators could be found liable for monetary damages. A finding of infringement could prevent us or our collaborators from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we or our collaborators have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Many of our employees, consultants or advisors are currently or were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. Other than the litigation initiated by the Leonard and Madlyn Abramson Family Cancer Research Institute at the Abramson Cancer Center of the University of Pennsylvania and by the Trustees of the University of Pennsylvania described above, no such claims have been filed against us to date.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patents for some of our technology and medicines, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. With respect to our proprietary cellular metabolism technology platform, we consider trade secrets and know-how to be our primary intellectual property. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that

with respect to this technology platform, these trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel skilled in the art from academic to industry scientific positions.

We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be harmed.

Table of Contents

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and comparable regulatory authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We and our collaborators have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we or our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved medicine not commercially viable.

Accordingly, if we or our collaborators experience delays in obtaining approval or if we or they fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenue will be materially impaired.

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

In the United States, AG-221 and AG-120 received fast track designation for treatment of patients with acute myelogenous leukemia, or AML, that harbor an IDH2 and IDH1 mutation, respectively. If a drug is intended for the treatment of a serious or life-threatening disease or condition and the drug demonstrates the potential to address unmet medical needs for this disease or condition, the drug sponsor may apply for FDA fast track designation. The FDA has

broad discretion whether or not to grant fast track designation, so even if we believe a particular product candidate is eligible for such designation, the FDA may decide not to grant it. Even though AG-221 and AG-120 have received fast track designation for treatment of patients with AML that harbor an IDH2 and IDH1 mutation, respectively, we may not experience a faster development process, review or approval, if at all, compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

Failure to obtain marketing approval in foreign jurisdictions would prevent our medicines from being marketed in such jurisdictions.

In order to market and sell our medicines in the European Union and many other jurisdictions, we or our collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, a product be approved for reimbursement before the product can be approved for sale in that country. We or our collaborators may not obtain approvals from regulatory authorities outside the

Table of Contents

United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any market.

Any product candidate for which we or our collaborators obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.

Any product candidate for which we or our collaborators obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our medicines for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our medicines, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

restrictions on such medicine, manufacturers or manufacturing processes;

restrictions on the labeling or marketing of a medicine;

restrictions on distribution or use of a medicine;

requirements to conduct post-marketing studies or clinical trials;

warning letters or untitled letters;

withdrawal of the medicine from the market;

refusal to approve pending applications or supplements to approved applications that we submit;

recall of medicines;

damage to relationships with any potential collaborators;

unfavorable press coverage and damage to our reputation;

fines, restitution or disgorgement of profits or revenue;

suspension or withdrawal of marketing approvals;

refusal to permit the import or export of our medicines;

product seizure;

injunctions or the imposition of civil or criminal penalties; and

litigation involving patients using our medicines.

Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the European Union's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Table of Contents

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at \$5,500 to \$11,000 per false claim;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals, with data collection beginning in August 2013; and

analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of our other product candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our other product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

Table of Contents

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and our product candidates are the following:

an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;

an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;

a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;

a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;

expansion of eligibility criteria for Medicaid programs;

expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

new requirements to report certain financial arrangements with physicians and teaching hospitals;

a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;

a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

a new Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs; and

a Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislation, will continue until 2025. In addition, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and may otherwise affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our medicines. Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent product labeling and post-marketing testing and other requirements.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the principal members of our management and scientific teams, each of whom is employed at will, meaning we or they may terminate the employment relationship at any time. We do not maintain key person insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Table of Contents

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co-founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately, disclose unauthorized activities to us, or comply with securities laws. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, including for illegal insider trading activities, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. Because we have not made any acquisitions to date, our ability to do so successfully is unproven. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders.

We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Table of Contents

Risks Related to Our Common Stock

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

establish a classified board of directors such that not all members of the board are elected at one time;

allow the authorized number of our directors to be changed only by resolution of our board of directors;

limit the manner in which stockholders can remove directors from the board;

establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;

require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;

limit who may call stockholder meetings;

authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a shareholder rights plan, or so-called poison pill, that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a

prescribed manner.

If securities analysts do not publish research or reports about our business or if they publish negative, or inaccurate, evaluations of our stock, the price of our stock and trading volume could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

An active trading market for our common stock may not be sustained.

Although our common stock is listed on the NASDAQ Global Select Market, an active trading market for our shares may not be sustained. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or sell their shares at all. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Table of Contents

The price of our common stock is likely to be volatile, which could result in substantial losses for purchasers of our common stock.

The trading price of our common stock has been, and may continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. For example, since January 1, 2014 the price of our common stock on the NASDAQ Global Select Market has ranged from \$21.70 per share to \$138.85 per share. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

regulatory actions with respect to our product candidates or our competitors' products and product candidates;

announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;

the timing and results of clinical trials of product candidates;

commencement or termination of collaborations for our development programs;

failure or discontinuation of any of our development programs;

results of clinical trials of product candidates of our competitors;

regulatory or legal developments in the United States and other countries;

developments or disputes concerning patent applications, issued patents or other proprietary rights;

the recruitment or departure of key personnel;

the level of expenses related to any of our product candidates or clinical development programs;

the results of our efforts to develop additional product candidates or products;

actual or anticipated changes in estimates as to financial results or development timelines;

announcement or expectation of additional financing efforts;

sales of our common stock by us, our insiders or other stockholders;

variations in our financial results or those of companies that are perceived to be similar to us;

changes in estimates or recommendations by securities analysts, if any, that cover our stock;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors;

general economic, industry and market conditions; and

the other factors described in this Risk Factors section.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Certain stockholders hold a substantial number of shares of our common stock. If such stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our stock incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act, and, in any event, we have filed a registration statement permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates. Any sales of securities by these stockholders who have exercised registration rights could have a material adverse effect on the trading price of our common stock.

Table of Contents

Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval.

As of March 31, 2016, our executive officers, directors and a small group of stockholders, in the aggregate, beneficially owned shares representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

Future sales and issuances of our common stock or rights to purchase common stock could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to those of holders of our common stock.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a company undergoes an ownership change, generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. Our prior equity offerings and other changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change. For example, in 2012, we completed a review of our changes in ownership through December 31, 2011, and determined that we had two qualified ownership changes since inception. The changes of ownership will result in net operating loss and research and development credit carryforwards that we expect to expire unutilized. If additional limitations were to apply, utilization of a portion of our net operating loss and tax credit carryforwards could be further limited in future periods and a portion of the carryforwards could expire before being available to reduce future income tax liabilities.

We incur increased costs as a result of operating as a public company, and our management is now required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly since January 1, 2015 when we ceased to be an emerging growth company, we have incurred and will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and will make some activities more time-consuming and costly. In addition, stockholder activism, the current political environment and the current high

level of government intervention and regulatory reform may lead to substantial new regulations.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish with our periodic Exchange Act reports a report by our management on our internal control over financial reporting and are required to include with our annual report an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404, we have engaged in a process to document and evaluate our internal control over financial reporting, which has been, and will continue to be, both costly and challenging. In this regard, we will need to continue to dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, from time to time, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Table of Contents

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Item 6. Exhibits.

The exhibits listed in the Exhibit Index to this Quarterly Report on Form 10-Q are incorporated herein by reference.

Table of Contents

SIGNATURES

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

AGIOS PHARMACEUTICALS, INC.

Date: May 9, 2016

By: */s/ David P. Schenkein*
David P. Schenkein

President and Chief Executive Officer

(principal executive officer)

Date: May 9, 2016

By: */s/ Glenn Goddard*
Glenn Goddard

Senior Vice President, Finance

(principal financial and accounting officer)

Table of Contents**EXHIBIT INDEX**

Exhibit	Description of Exhibit	Incorporated by Reference			Exhibit Number	Filed Herewith
		Form	File Number	Date of Filing		
3.1	Restated Certificate of Incorporation	8-K	001-36014	July 29, 2013	3.1	
3.2	Amended and Restated By-Laws	8-K	001-36014	July 29, 2013	3.2	
10.1	Letter Agreement, dated as of January 7, 2016, between the Registrant and Steve Hoerter					X
10.2	Severance Benefits Plan	8-K	001-36014	April 22, 2016	10.1	
31.1	Certification of principal executive officer pursuant to Rule 13a 14(a)/15d 14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	XBRL Instance Document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Label Linkbase Document					X
101.PRE	XBRL Taxonomy Presentation Linkbase Document					X

