AGIOS PHARMACEUTICALS INC
Form 10-Q
November 07, 2014
**Table of Contents**

**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

**Washington, DC 20549**

# FORM 10-Q

**(Mark One)**

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

**For the quarterly period ended September 30, 2014**

**OR**

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

**Commission file number 001-36014**

**AGIOS PHARMACEUTICALS, INC.**

**(Exact Name of Registrant as Specified in Its Charter)**

| **Delaware** | **26-0662915** |
|---|---|
| **(State or Other Jurisdiction of Incorporation or Organization)** | **(I.R.S. Employer Identification No.)** |
| **38 Sidney Street, 2nd Floor, Cambridge, Massachusetts** | **02139** |
| **(Address of Principal Executive Offices)** | **(Zip Code)** |

**(617) 649-8600**

**(Registrant s Telephone Number, Including Area Code)**

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

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

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

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

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

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

Number of shares of the registrant s Common Stock, $0.001 par value, outstanding on November 6, 2014: 34,683,082

Table of Contents

**AGIOS PHARMACEUTICALS, INC.**

**FORM 10-Q**

**FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2014**

**TABLE OF CONTENTS**

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)***

| | September 30, 2014 | December 31, 2013 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 70,049 | $ 71,560 |
| Marketable securities | 149,921 | 95,209 |
| Collaboration receivable related party | 18,759 | 476 |
| Prepaid expenses and other current assets | 4,990 | 2,502 |
| Refundable income taxes | 3,841 | |
| Total current assets | 247,560 | 169,747 |
| Marketable securities | 17,917 | 27,125 |
| Property and equipment, net | 3,677 | 3,758 |
| Restricted cash | | 571 |
| Other assets | 454 | 4 |
| Total assets | $ 269,608 | $ 201,205 |
| **Liabilities and stockholders equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 6,225 | $ 3,678 |
| Accrued expenses | 10,004 | 6,586 |
| Income taxes payable | | 1,462 |
| Deferred revenue related party | 18,847 | 25,072 |
| Deferred rent | | 123 |
| Other current liabilities | 8 | 9 |
| Total current liabilities | 35,084 | 36,930 |
| Deferred revenue, net of current portion related party | 26,352 | 32,567 |
| Deferred rent, net of current portion | 423 | 220 |
| Other non-current liabilities | | 6 |
| Commitments and contingencies | | |
| Stockholders equity: | | |

| | | |
|---|---|---|
| Preferred stock, $0.001 par value; 25,000,000 shares authorized; no shares issued and outstanding | | |
| Common stock, $0.001 par value; 125,000,000 shares authorized; 34,642,539 and 31,202,542 shares issued and outstanding at September 30, 2014 and December 31, 2013, respectively | 35 | 31 |
| Additional paid-in capital | 347,947 | 244,881 |
| Accumulated other comprehensive income | 51 | 14 |
| Accumulated deficit | (140,284) | (113,444) |
| Total stockholders equity | 207,749 | 131,482 |
| Total liabilities and stockholders equity | $ 269,608 | $ 201,205 |

*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 September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | **2014** | **2013** | **2014** | **2013** |
| Gross Collaboration revenue related party | $ 33,900 | $ 6,268 | $ 50,722 | $ 18,804 |
| Operating expenses: | | | | |
| Research and development | 25,526 | 14,803 | 65,509 | 39,223 |
| General and administrative | 5,166 | 2,534 | 12,619 | 6,222 |
| Total operating expenses | 30,692 | 17,337 | 78,128 | 45,445 |
| Income (loss) from operations | 3,208 | (11,069) | (27,406) | (26,641) |
| Interest income | 48 | 13 | 118 | 26 |
| Income (loss) before (benefit) provision for income taxes | 3,256 | (11,056) | (27,288) | (26,615) |
| (Benefit) provision for income taxes | (448) | 121 | (448) | 410 |
| Net income (loss) | 3,704 | (11,177) | (26,840) | (27,025) |
| Cumulative preferred stock dividends | | (567) | | (4,162) |
| Net income (loss) applicable to common stockholders | $ 3,704 | $ (11,744) | $ (26,840) | $ (31,187) |
| Net income (loss) per share applicable to common stockholders basic | $ 0.11 | $ (0.52) | $ (0.81) | $ (3.08) |
| Net income (loss) per share applicable to common stockholders diluted | $ 0.10 | $ (0.52) | $ (0.81) | $ (3.08) |
| Weighted-average number of common shares used in net income (loss) per share applicable to common stockholders basic | 34,495,076 | 22,744,486 | 33,176,801 | 10,111,735 |
| Weighted-average number of common shares used in net income (loss) per share applicable to common stockholders diluted | 36,592,683 | 22,744,486 | 33,176,801 | 10,111,735 |

*See accompanying notes to condensed consolidated financial statements.*

4

Table of Contents

**AGIOS PHARMACEUTICALS, INC.**

**Condensed Consolidated Statements of Comprehensive Income (Loss)**

**(in thousands)**

***(Unaudited)***

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | **2014** | **2013** | **2014** | **2013** |
| Net income (loss) | $ 3,704 | $ (11,177) | $ (26,840) | $ (27,025) |
| Other comprehensive income: | | | | |
| Unrealized gain on available-for-sale securities | 39 | 30 | 37 | 27 |
| Comprehensive income (loss) | $ 3,743 | $ (11,147) | $ (26,803) | $ (26,998) |

*See accompanying notes to condensed consolidated financial statements.*

Table of Contents

**AGIOS PHARMACEUTICALS, INC.**

**Condensed Consolidated Statements of Cash Flows**

**(in thousands)**

***(Unaudited)***

| | Nine Months Ended September 30, | |
|---|---|---|
| | **2014** | **2013** |
| **Operating activities** | | |
| Net loss | $ (26,840) | $ (27,025) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | |
| Depreciation | 1,005 | 1,100 |
| Stock-based compensation expense | 6,778 | 1,865 |
| Net amortization of premium on investments | 412 | 81 |
| Changes in operating assets and liabilities: | | |
| Collaboration receivable related party | (18,283) | |
| Prepaid expenses and other assets | (2,756) | (1,684) |
| Accounts payable | 2,354 | (1,178) |
| Accrued expenses and other liabilities | 3,414 | 2,480 |
| Deferred rent | 80 | |
| Refundable income taxes and income taxes payable | (5,303) | 382 |
| Deferred revenue related party | (12,439) | (18,804) |
| Net cash used in operating activities | (51,578) | (42,783) |
| **Investing activities** | | |
| Purchases of marketable securities | (215,383) | (119,498) |
| Proceeds from maturities and sales of marketable securities | 169,505 | 53,766 |
| Purchases of property and equipment | (727) | (1,075) |
| Release of restricted cash | 571 | |
| Net cash used in investing activities | (46,034) | (66,807) |
| **Financing activities** | | |
| Proceeds from public offering of common stock, net of commissions and offering costs | 94,685 | 124,204 |
| Net proceeds from stock option exercises and issuance of common stock | 1,416 | 100 |
| Net cash provided by financing activities | 96,101 | 124,304 |
| Net increase (decrease) in cash and cash equivalents | (1,511) | 14,714 |
| Cash and cash equivalents at beginning of the period | 71,560 | 91,297 |
| Cash and cash equivalents at end of the period | $ 70,049 | $ 106,011 |
| **Supplemental disclosure of non-cash investing and financing transactions** | | |

| | | | | |
|---|---|---|---|---|
| Additions to property, plant and equipment included in accounts payable | $ | 197 | $ | |
| Vesting of restricted stock | | (7) | | |
| Conversion of convertible preferred stock into common stock | | | | 115,923 |
| Public offering costs included in accounts payable | | | | 474 |
| Proceeds from stock option exercises in other current assets | | 184 | | |
| **Supplemental cash flow information** | | | | |
| Cash paid for income taxes | $ | 5,958 | $ | |

*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

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 disorders of metabolism. 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. The Company s therapeutic areas of focus are cancer and rare genetic disorders of metabolism, 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.

The condensed consolidated interim balance sheet as of September 30, 2014, the condensed consolidated interim statements of operations and comprehensive income (loss) for the three and nine months ended September 30, 2014 and 2013 and the statements of cash flows for the nine months ended September 30, 2014 and 2013, 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 September 30, 2014 and its results of operations for the three and nine months ended September 30, 2014 and 2013 and cash flows for the nine months ended September 30, 2014 and 2013. The financial data and the other financial information disclosed in these notes to the condensed consolidated interim financial statements related to the three and nine month periods are also unaudited. The results of operations for the three and nine months ended September 30, 2014 are not necessarily indicative of the results to be expected for the year ending December 31, 2014 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, 2013 that was filed with the Securities and Exchange Commission (the SEC ) on March 18, 2014.

The Company s condensed consolidated financial statements include the Company s accounts and the accounts of the Company s wholly-owned subsidiary, Agios Securities Corporation. All intercompany transactions have been eliminated in consolidation. The condensed consolidated interim financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ( GAAP ).

On July 29, 2013, the Company closed an initial public offering ( IPO ) of its common stock, which resulted in the sale of 6,772,221 shares of its common stock at a public offering price of $18.00 per share, before underwriting commissions and discounts, including 883,333 shares of common stock issued upon the exercise in full by the underwriters of their option to purchase additional shares at the public offering price to cover over-allotments. The Company received net proceeds from the IPO of $111.0 million, after deducting underwriting discounts, commissions, and expenses payable by the Company. Additionally, an affiliate of Celgene Corporation ( Celgene ), the Company s cancer metabolism strategic alliance partner, purchased 708,333 shares of common stock in a separate private placement concurrent with the completion of the IPO at a purchase price of $18.00 per share for aggregate proceeds of $12.8 million.

In connection with preparing for the IPO, the Company s Board of Directors and stockholders approved a 1-for-2.75 reverse stock split of the Company s common stock. The reverse stock split became effective on July 11, 2013. All share and per share amounts in the condensed consolidated interim financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital. In connection with the closing of the IPO, all of the Company s outstanding convertible preferred stock automatically converted to common stock as of July 29, 2013, resulting in an additional 19,731,564 shares of common stock of the Company becoming outstanding.

In April 2014, the Company completed a public offering of 2,000,000 shares of its common stock at a public offering price of $44.00 per share, before underwriting commissions and discounts. The Company received net proceeds from this offering of $82.3 million, after deducting underwriting discounts, commissions and expenses payable by the Company. Celgene purchased 294,800 shares of the Company s common stock in the offering. In addition, the Company granted the underwriters the right to purchase up to an additional 300,000 shares of its common stock which was exercised in May 2014 resulting in additional net proceeds to the Company of $12.4 million, after underwriting discounts and commissions paid by the Company.

Table of Contents

**2. Summary of Significant Accounting Policies and Recent Accounting Pronouncements**

In July 2014, the Company amended its collaboration agreement with Celgene. As a result of the amendment, the Company was required to reevaluate the agreement under Financial Accounting Standards Board ( FASB ) Accounting Standards Update ( ASU ) No. 2009-13, *Multiple-Element Revenue Arrangements* ( ASU No. 2009-13 ). The amendment was determined to be a material modification pursuant to ASU No. 2009-13, and the Company will recognize revenue for the arrangement under this guidance on a prospective basis, as discussed in Note 5.

There have been no other material changes to the significant accounting policies previously disclosed in the Annual Report on Form 10-K for the year ended December 31, 2013.

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 June 2014, the FASB issued ASU No. 2014-12, *Compensation Stock Compensation (Topic 718)*. The ASU clarifies how entities should treat performance targets that can be achieved after the requisite service period of a share-based payment award. The accounting standard is effective for interim and annual periods beginning after December 15, 2015 and is not expected to have a material impact on the consolidated financial statements.

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. 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 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 ) Topic 820, *Fair Value Measurements and Disclosures*, established 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, either 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 September 30, 2014 (in thousands):

| | Level 1 | Level 2 | Level 3 | Total |
|---|---|---|---|---|
| Cash equivalents | $ 69,245 | $ 480 | $ | $ 69,725 |
| Marketable securities: | | | | |
| Certificates of deposit | | 14,521 | | 14,521 |
| U.S. Treasuries | 153,317 | | | 153,317 |
| | $ 222,562 | $ 15,001 | $ | $ 237,563 |

Table of Contents

The following table summarizes the cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2013 (in thousands):

| | Level 1 | Level 2 | Level 3 | Total |
|---|---|---|---|---|
| Cash equivalents | $ 68,792 | $ | $ | $ 68,792 |
| Marketable securities: | | | | |
| Certificates of deposit | | 6,915 | | 6,915 |
| U.S. Treasuries | 115,419 | | | 115,419 |
| | $ 184,211 | $ 6,915 | $ | $ 191,126 |

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. The Company validates the prices provided by its third-party pricing services by reviewing their pricing methods and obtaining market values from other pricing sources. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by the pricing services as of September 30, 2014 or December 31, 2013.

There have been no changes to the valuation methods during the three or nine months ended September 30, 2014 and 2013. 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 and nine months ended September 30, 2014 or the year ended December 31, 2013. The Company had no financial assets or liabilities that were classified as Level 3 at any point during the nine months ended September 30, 2014 or the year ended December 31, 2013.

**4. Marketable Securities**

Marketable securities at September 30, 2014 and December 31, 2013 consisted primarily of investments in United States Treasuries and certificates of deposit. 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 income in stockholders equity and a component of total comprehensive income (loss) in the condensed consolidated interim statements of comprehensive income (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 or nine months ended September 30, 2014 and 2013.

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.

Marketable securities at September 30, 2014 consist of the following (in thousands):

| | Amortized Cost | Unrealized Gains | Unrealized Losses | Fair Value |
|---|---|---|---|---|
| Current: | | | | |
| Certificates of deposit | $ 14,530 | $ | $ (9) | $ 14,521 |
| U.S. Treasuries | 135,348 | 53 | (1) | 135,400 |
| Non-current: | | | | |
| U.S. Treasuries | 17,909 | 8 | | 17,917 |
| | $ 167,787 | $ 61 | $ (10) | $ 167,838 |

Table of Contents

Marketable securities at December 31, 2013 consist of the following (in thousands):

| | Amortized Cost | Unrealized Gains | Unrealized Losses | Fair Value |
|---|---|---|---|---|
| Current: | | | | |
| Certificates of deposit | $ 6,920 | $ | $ (5) | $ 6,915 |
| U.S. Treasuries | 88,287 | 8 | (1) | 88,294 |
| Non-current: | | | | |
| U.S. Treasuries | 27,113 | 12 | | 27,125 |
| | $ 122,320 | $ 20 | $ (6) | $ 122,334 |

At September 30, 2014 and December 31, 2013, 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 maturities 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.

At September 30, 2014 and December 31, 2013, the Company held 60 and 33 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 September 30, 2014 and December 31, 2013 was $21.5 million and $31.7 million, respectively. There were no individual securities that were in a significant unrealized loss position as of September 30, 2014 and December 31, 2013. 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 September 30, 2014 and December 31, 2013.

**5. Collaboration Agreements**

***Celgene***

In April 2010, the Company entered into a collaboration agreement focused on cancer metabolism with Celgene, a related party through ownership of the Company s common stock. The agreement was amended in October 2011 and in July 2014, as described below. 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 is leading discovery, preclinical and early clinical development for all cancer metabolism programs under the collaboration. The discovery phase of the amended collaboration was 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. Celgene has the ability to extend the term of the discovery phase for one additional year to April 2016 for the payment of a $20.0 million extension fee.

Pursuant to the collaboration agreement and subsequent amendments, the Company was 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 and during the year ended December 31, 2013 the Company nominated its second development candidate, both of

which have been confirmed by the JRC pursuant to the agreement. For each development candidate, Celgene elected to progress such development candidate into preclinical development requiring 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 INDs for each development candidate and, upon the FDA s acceptance of the INDs, Celgene requested that the Company conduct initial phase 1 studies.

Table of Contents

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. If Celgene exercises its rights to this program, the program will become a split licensed program. 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 Company will retain the rights to development candidates and certain other compounds that Celgene does not elect to progress into preclinical development or convert into a co-commercialized licensed program. In addition, if the JRC or Celgene elects not to continue collaboration activities with respect to a particular target, either the Company or Celgene would have the right to independently undertake a discovery program on such target and would have rights to specified compounds from such program, subject to certain buy-in rights granted to the other party.

The agreement provides for three types of licensed programs as discussed above:

*Co-Commercialized Licensed Programs*: Celgene will lead and, following either IND acceptance by the FDA or, if Celgene requests the Company to conduct the initial phase 1 study upon completion of such phase 1 study, will fund global development and commercialization. The Company has the right to participate in a portion of sales activities in the United States for products from co-commercialized programs in accordance with the applicable commercialization plan. The Company will be eligible to receive milestone payments and royalties arising from the licensed program.

*Split Licensed Programs*: Celgene will lead development and commercialization outside the United States and the Company will lead development and commercialization in the United States. The Company and Celgene will equally fund the global development costs of each split licensed program that are not specific to any particular region or country, Celgene will be responsible for development and commercialization costs specific to countries outside the United States, and the Company will be responsible for development and commercialization costs specific to the United States. The Company will retain profits generated in the United States and will also be eligible to receive milestone payments and royalties arising from net sales outside the United States. The Company will be obligated to pay Celgene royalties arising from net sales in the United States.

*Buy-In Programs:* If a party elects to independently undertake a discovery program, with respect to a particular target under the agreement, the party that is conducting the independent program that becomes a buy-in program will lead the development and commercialization of such program. The party that elects to buy in to such program will be responsible for funding a portion of development costs incurred after acceptance of an IND for a buy-in program compound, and the lead party will be responsible for all other development costs and all commercialization costs for products from such buy-in program. The commercializing party will be obligated to pay the buy-in party specified royalties on worldwide net sales.

The term of the agreement will continue, unless earlier terminated by either party, until the expiration of the last-to-expire of all royalty terms with respect to all royalty-bearing products. Celgene may terminate the agreement for convenience in its entirety or with respect to one or more programs upon thirty days written notice to the Company. Either the Company or Celgene may terminate the agreement in its entirety or with respect to one or more programs, if the other party is in material breach and fails to cure such breach within the specified cure period;

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.

Under the terms of the agreement, the Company received an upfront payment of approximately $121.2 million. In addition, Celgene purchased 5,190,551 shares of Series B convertible preferred stock ( Series B Preferred Stock ) at a price of $1.70 per share, resulting in net proceeds to the Company of approximately $8.8 million. The Company determined the price paid by Celgene for the Series B Preferred Stock represented a premium over the fair value of the Company s Series B Preferred Stock as determined by the implied value of the Series B Preferred Stock pursuant to a contemporaneous valuation analysis that allocated the equity value of the Company to the various classes of its then-outstanding securities. The Company accounted for the $3.1 million premium as additional consideration under the agreement and the Series B Preferred Stock was recorded at its fair value of $5.7 million. In connection with the 1-for-2.75 reverse stock split of the Company s common stock, the shares of Series B Preferred Stock converted into 1,887,473 shares of common stock upon the closing of the Initial Public Offering in July 2013.

Table of Contents

In October 2011, the agreement was amended to extend the term of the initial discovery period from three to four years, to April 2014. The amendment was not deemed to be a material modification to the arrangement, pursuant to ASU No. 2009-13, since there were no changes in the deliverables or the total arrangement consideration, as the provisions of the original agreement provided Celgene with the option to extend the research period for the same consideration. Celgene made a payment to the Company of $20.0 million pursuant to the amendment. The payment was combined with the unamortized upfront payment and premium and was recognized as revenue on a straight-line basis over the estimated performance period prior to the July 2014 amendment described below.

In December 2013, Celgene elected to extend the term of the initial discovery period from four to five years, to April 2015. As a result of the extension, the Company received a $20.0 million extension payment from Celgene in May 2014. The payment was combined with the unamortized upfront payment, premium, and prior extension payment and was being recognized as revenue on a straight-line basis over the estimated performance period prior to the July 2014 amendment described below. The Company is also eligible to receive an additional $20.0 million extension payment in the event Celgene elects to extend the discovery phase until April 2016.

In July 2014, the Company amended the collaboration agreement to allow for more flexibility in the design and conduct of phase 1 clinical trials and additional nonclinical and/or clinical activities that the Company agrees to perform at Celgene s request. The amendment further modifies the mechanism and timing for payments to be made with respect to such development activities. The amendment was determined to be a material modification pursuant to ASU No. 2009-13, due to a change in the total potential consideration that was more than insignificant and changes to certain of the deliverables in the arrangement. The amendment impacts the co-commercialized and split licensed programs as follows:

Co-commercialized licensed programs: The amendment modifies the timing and nature of the consideration for the development efforts related to an initial phase 1 study from a milestone due at the completion of the study to payments due upon the earlier of the determination of the maximum tolerated dose or Celgene s election to license the program.

Split licensed programs: The amendment allows for the Company to receive reimbursement for costs and expenses it incurs for any disease-specific expansion cohort within a phase 1 clinical trial design, provided that the disease-specific expansion cohort supports the initiation of a subsequent pivotal clinical trial. The milestone reimbursement is the lesser of fifty percent of the costs incurred by the Company for disease specific cohorts and $10 million and is payable upon the first patient dosed within the corresponding pivotal trial.

Prior to the amendment, 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 agreement. Consideration received was 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 6 years.

Upon concluding the arrangement had been materially modified in July 2014, the Company identified the remaining deliverables under the arrangement and determined its 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 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 allocable consideration and the best estimate of selling price of the undelivered items was recorded as revenue at

the modification date. 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, and the method of recognizing the allocated consideration, for each unit of accounting are 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. Management estimates within the models include the expected, probability-weighted net profits from estimated future sales, an estimated royalty rate using comparable industry royalty agreements, an estimate of the direct cost incurred to generate future cash flows, a discount rate, an estimated contributory asset charge rate to reflect the cost associated with the use of other assets to generate the cash flow, an estimated income tax rate and other business forecast factors. There are significant judgments and estimates inherent in the determination of the best estimate of selling price of this unit 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 revenues recognized would be different. Based on the analysis using management s best estimate, the Company allocated $21.2 million to the license and will recognize revenue upon Celgene s election to exercise its option to the split licensed program AG-120. The Company will immediately recognize the allocated consideration received to date on the exercise date; however, the Company is unable to determine when Celgene will elect to exercise its option to obtain the license.

Table of Contents

Development services for five separate on-going phase 1 studies (each of which is a separate unit of accounting): The Company developed the best estimate of selling price of the on-going phase 1 study development services of $50.8 million for all five studies using management s best estimate of the cost of obtaining these services from a third-party provider. The estimated costs were determined to represent management s best estimate of the price these services could be sold for separately, as well as internal full time equivalent costs to support the development services. The amount allocated to these units of accounting will be recognized as revenue on a proportional performance basis as services are provided. The Company expects the performance period for these units of accounting to be delivered through the second quarter of 2016.

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 from a third-party provider. The amount allocated to this unit of accounting will be recognized as revenue ratably over the performance period. The performance period has been determined to be through April 2015.

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 will be recognized as revenue ratably over the performance period. The performance period has been determined to be through April 2015.

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.

For the period January 1, 2014 through the amendment date, the Company recognized a total of $42.7 million in revenues under the previous accounting guidance and upon the modification. The Company recognized $8.0 million in revenues subsequent to the modification date. The Company recognized total revenues of $33.9 million and $50.7 million in connection with the Celgene collaboration during the three and nine months ended September 30, 2014, respectively. 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.

Table of Contents

The Company recorded revenue of approximately $6.3 million and $18.8 million in connection with the Celgene collaboration during the three and nine months ended September 30, 2013, respectively.

Under the arrangement, 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. 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 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 (MAD) study. 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 (MTD) or Celgene s election to license the program. Subsequent to the initial milestone payment, development costs will be reimbursed on a quarterly basis. As of September 30, 2014, the Company has recorded a collaboration receivable of $18.7 million related to reimbursable development costs for AG-221, which includes the initial milestone.

In addition to the milestone payments described above, for each split licensed program, 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. The maximum amount for the milestone payment will be $10.0 million for each split program regardless of the number of disease-specific expansion cohorts and pivotal trials undertaken for each split program.

The Company has concluded that certain of the clinical development and regulatory milestones that may be received under the Celgene agreement, 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. Revenues 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.

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 are recognized as revenue in the period in which they are earned. No other milestone or royalty payments under the agreement have been earned.

14

Table of Contents

**6. Accrued Expenses and Other Current Liabilities**

Accrued expenses and other current liabilities consist of the following (in thousands):

| | September 30, 2014 | December 31, 2013 |
|---|---|---|
| Accrued compensation | $ 3,273 | $ 3,642 |
| Accrued contracted research and development costs | 4,425 | 2,484 |
| Accrued professional fees | 1,271 | 320 |
| Accrued other | 1,035 | 140 |
| Total | $ 10,004 | $ 6,586 |

**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 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-based awards. As of September 30, 2014, the total number of shares reserved under all equity plans is 4,616,104 and the Company had 799,270 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, 2014, the annual increase for the 2013 Plan resulted in an additional 1,242,966 shares authorized for issuance.

The following table summarizes the activity of all stock incentive plans for the nine months ended September 30, 2014:

| | Number of Stock Options | Weighted-Average Exercise Price | Weighted-Average Remaining Contractual Term (in years) | Aggregate Intrinsic Value (in thousands) |
|---|---|---|---|---|
| Outstanding at December 31, 2013 | 3,846,168 | $ 4.14 | 7.43 | $ 76,189 |
| Granted | 1,176,733 | 33.23 | | |
| Exercised | (1,128,065) | 1.42 | | |
| Forfeited/cancelled | (78,002) | 12.75 | | |
| Outstanding at September 30, 2014 | 3,816,834 | $ 13.74 | 7.70 | $ 181,726 |

| | | | | | |
|---|---|---|---|---|---|
| Exercisable at September 30, 2014 | 1,635,445 | $ 2.02 | 6.01 | $ | 97,023 |
| Vested and expected to vest at September 30, 2014 | 3,373,444 | $ 13.67 | 7.57 | $ | 160,838 |

The weighted-average grant date fair value of options granted was $31.14, $16.30, $24.30 and $9.83 during the three months ended September 30, 2014 and 2013 and the nine months ended September 30, 2014 and 2013, respectively. The total intrinsic value of options exercised was $10 million, $0.2 million, $44.8 million, and $0.6 million during the three months ended September 30, 2014 and 2013 and the nine months ended September 30, 2014 and 2013, respectively.

At September 30, 2014, the total unrecognized compensation expense related to unvested stock option awards, including estimated forfeitures, was $27.4 million, which the Company expects to recognize over a weighted-average period of approximately 3.1 years. The Company also has unrecognized stock-based compensation expense of $2.8 million related to stock options with performance-based vesting criteria that are not considered probable of achievement as of September 30, 2014; therefore the Company has not yet begun to recognize the expense on these awards.

*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. The total number of unvested RSUs at September 30, 2014 was 10,000. The issued and outstanding RSUs vest on the first anniversary of the grant date.

Table of Contents

The fair value of the RSUs granted in the three and nine months ended September 30, 2014 was approximately $0.5 million. No RSUs were granted in the three and nine months ended September 30, 2013. The Company recorded stock-based compensation expense related to RSUs of $0.1 million for the three and nine months ended September 30, 2014. No compensation expense related to RSUs was recorded during 2013. These amounts are included in the total stock-based compensation expense disclosed below. As of September 30, 2014, there was approximately $0.5 million of total unrecognized compensation expense related to RSUs, which is expected to be recognized over a period of one year.

The following table presents unvested RSU activity for the nine months ended September 30, 2014:

| | Nine Months Ended September 30, 2014 |
|---|---|
| Unvested shares beginning of period | |
| Granted | 10,000 |
| Vested | |
| Unvested shares end of period | 10,000 |

*Restricted Stock*

At September 30, 2014, there were 11,363 shares of unvested restricted stock which remain subject to the Company s right of repurchase.

Unvested restricted stock activity for the nine months ended September 30, 2014 is summarized as follows:

| | Nine Months Ended September 30, 2014 |
|---|---|
| Unvested shares beginning of period | 23,295 |
| Vested | (11,932) |
| Unvested shares end of period | 11,363 |

*Performance-Based Stock Option Grants*

During the nine months ended September 30, 2014, no options to purchase shares of common stock were granted which contain performance-based or a combination of performance-based and service-based vesting criteria. During the nine months ended September 30, 2013, the Company granted 355,454 shares of common stock, which contain performance-based and service-based vesting criteria, to employees. Performance-based vesting criteria for these 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 September 30, 2014, certain of the performance-based milestones had been achieved and therefore the related expense has either 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 September 30, 2014 and therefore no expense has been recognized related to these awards. During the three months ended September 2014 and 2013 and nine months ended September 2014 and 2013, the Company recognized stock-based compensation expense of $0.1 million, $0.1 million, $0.1 million, and $0.3 million, respectively, related to stock options with performance-based vesting criteria.

Table of Contents

***Stock-Based Compensation Expense***

During the three and nine months ended September 30, 2014 and 2013, the Company recorded stock-based compensation expense for employee and non-employee stock options, restricted stock units and restricted stock, which was allocated as follows in the condensed consolidated interim statements of operations (in thousands):

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2014 | 2013 | 2014 | 2013 |
| Research and development expense | $ 1,438 | $ 919 | $ 3,899 | $ 1,452 |
| General and administrative expense | 1,428 | 193 | 2,853 | 413 |
| | $ 2,866 | $ 1,112 | $ 6,752 | $ 1,865 |

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 September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2014 | 2013 | 2014 | 2013 |
| Risk-free interest rate | 1.95% | 1.73% | 1.83% | 1.23% |
| Expected dividend yield | | | | |
| Expected term (in years) | 6.00 | 6.09 | 6.02 | 6.36 |
| Expected volatility | 78.89% | 94.25% | 84. 77% | 92.60% |

***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 will be 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 s first offering period was initiated on September 1, 2014. No shares were issued for the three and nine months ended September 30, 2014 under the 2013 ESPP. The 2013 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 327,272 shares of the Company s common stock.

The Company recorded less than $0.1 million of stock-based compensation expense for the three months ended September 30, 2014 related to the 2013 ESPP. No stock-based compensation expense related to the 2013 ESPP was recorded during 2013.

**8. Income Taxes**

The (benefit) provision for income taxes is as follows for the three and nine months ended September 30, 2014 and 2013 (in thousands):

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2014 | 2013 | 2014 | 2013 |
| Current: | | | | |
| Federal | $ (448) | $ 121 | $ (448) | $ 410 |
| State | | | | |
| Total current | (448) | 121 | (448) | 410 |
| Deferred: | | | | |
| Federal | | | | |
| State | | | | |
| Total deferred | | | | |
| Total | $ (448) | $ 121 | $ (448) | $ 410 |

As required by ASC 740, Income Taxes ( ASC 740 ), management of the Company has evaluated the positive and negative evidence bearing upon the realizability of the Company s deferred tax assets, which are comprised principally of timing differences related to the recognition of revenue under the Celgene Agreement for financial statement versus tax purposes. During the year ended December 31, 2011, management determined that it was more likely than not that it would realize a

Table of Contents

portion of its deferred tax assets because of the Company s ability to carryback future losses for U.S. federal income tax purposes. As a result, the Company reversed approximately $10.7 million of the valuation allowance on its deferred tax assets in the year ended December 31, 2011, representing the amount of deferred tax assets that would be realized in 2012 and 2013, the years available for carryback. The Company utilized certain of the deferred tax assets, including net operating losses, generated in the years ended December 31, 2013 and 2012 to reduce its federal income taxes payable each year. The provision for income taxes for the three and nine months ended September 30, 2013 was attributable to penalties and interest accrued for the non-payment of U.S. federal 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 has filed a carryback claim to apply the net losses incurred during the year ended December 31, 2013 against the previous taxable income and expects to receive a refund of $3.8 million of the amounts paid in January 2014 after the filing of the Company s 2013 tax return which occurred in September 2014. The amount expected to be refunded by the Internal Revenue Service ( IRS ) is recorded as refundable income taxes as of September 30, 2014. The Company received abatements from the IRS of $1.1 million related to penalties previously paid by the Company of which $0.7 million was received in June 2014 and $0.4 million was received during the three months ended September 30, 2014. The $0.7 million abatement was known as of December 31, 2013 and was recorded as a benefit in the 2013 tax provision. The Company did not receive notification of the $0.4 million abatement until August 2014. Accordingly, this abatement is reflected in the income tax benefit for the three months ended September 30, 2014.

The Company applies the accounting guidance in ASC 740 related to accounting for uncertainty in income taxes. The Company s reserves related to taxes are based on a determination of whether, and how much of, a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. As of September 30, 2014, the Company had no unrecognized tax benefits. The Company recognizes interest and penalties related to uncertain tax positions in the (benefit) provision for income taxes.

**9. Earnings per Share Applicable to Common Stockholders**

Basic net income (loss) per share applicable to common stockholders is calculated by dividing net income (loss) applicable to common stockholders by the weighted-average shares outstanding during the period, without consideration for common stock equivalents. Net income (loss) applicable to common stockholders is calculated by adjusting the net income (loss) of the Company for cumulative preferred stock dividends for periods when preferred stock was outstanding.

Diluted net income per share applicable to common stockholders 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 calculating diluted net loss per share applicable to common stockholders, common stock equivalents outstanding for the period are excluded, as their effect would be anti-dilutive.

The following table shows the calculation of basic and diluted earnings per share for the three and nine month periods ended September 30, 2014 and September 30, 2013 (in thousands, except share and per share data):

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2014 | 2013 | 2014 | 2013 |
| | 3,704 | (11,744) | (26,840) | (31,187) |

| | | | | |
|---|---|---|---|---|
| Net income (loss) applicable to common stockholders | | | | |
| Weighted-average shares: | | | | |
| Basic | 34,495,076 | 22,744,486 | 33,176,801 | 10,111,735 |
| Effect of dilutive securities: | | | | |
| Stock options and restricted stock units | 2,085,068 | | | |
| Unvested restricted stock | 12,523 | | | |
| Employee stock purchase plan options | 16 | | | |
| Diluted | 36,592,683 | 22,744,486 | 33,176,801 | 10,111,735 |
| Net income (loss) per share: | | | | |
| Basic | 0.11 | (0.52) | (0.81) | (3.08) |
| Diluted | 0.10 | (0.52) | (0.81) | (3.08) |

The following potentially dilutive securities were excluded from the calculation of diluted net income (loss) per share applicable to common stockholders for the periods indicated because their effect would have been anti-dilutive:

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| | 2014 | 2013 | 2014 | 2013 |
| Stock options and restricted stock units | 1,484,917 | 3,905,932 | 3,816,834 | 3,905,932 |
| Unvested restricted stock | | 36,568 | 11,363 | 36,568 |
| Employee stock purchase plan options | | | 1,764 | |
| | 1,484,917 | 3,942,500 | 3,829,961 | 3,942,500 |

**10. Commitments and Contingencies**

***Operating Lease***

On September 15, 2014, the Company entered into an operating lease agreement (the Lease ) for 74,498 square feet of office and laboratory space located at 88 Sidney Street, Cambridge, Massachusetts. The Company also entered into an agreement to terminate its existing lease under which the Company currently leases 38,536 square feet of office and laboratory space located at 38 Sidney Street, Cambridge, Massachusetts. The Company s existing lease will terminate thirty days after the Commencement Date. The date on which the Company will become responsible for paying rent under the Lease (the Commencement Date ) will be the earlier of May 15, 2015 or the date upon which the Company first begins conducting business at the new location. The Company s existing lease will terminate thirty days after the Commencement Date. The initial lease term will be for a period of seven years from the Commencement Date. At the end of the lease term, the Company has the option to extend the Lease for two consecutive terms of five years at fair market rent at the time of the extension. The Lease agreement includes rent escalation clauses, a tenant improvement allowance of $11.2 million and access to temporary space located at the premises for no cost. The Company gained physical access to the leased space in September 2014 and began to record rent expense on a straight-line basis over the effective term of the Lease. The Company provided a standby letter of credit of $1.4 million as security for its obligations under the Lease which was issued in October 2014.

Future annual minimum lease payments due under the new and existing operating leases at December 31 of each year are as follows (in thousands):

| | |
|---|---|
| 2014 | $ 677 |
| 2015 | 3,538 |
| 2016 | 4,318 |
| 2017 | 4,405 |
| 2018 | 4,493 |
| Thereafter | 15,826 |
| | $ 33,257 |

Rent expense was $0.7 million and $0.5 million for the three months ended September 30, 2014 and 2013, respectively and was $1.8 million and $1.6 million for the nine months ended September 30, 2014 and 2013, respectively. The operating leases require the Company to share in prorated operating expenses and property taxes based upon actual amounts incurred; those amounts are not fixed for future periods and, therefore, are not included in the future commitments listed above.

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 September 30, 2014 and for the three and nine months ended September 30, 2014 and 2013 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, 2013 filed with the SEC on March 18, 2014. 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, plan, predict, project, target, potential, will, would, could, should, continue, and similar statement 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 with rare genetic disorders of metabolism, 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 believe that dysregulation of normal cellular metabolism plays a crucial role in many diseases, including certain cancers and rare genetic disorders. 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 for cancer and rare genetic disorders.

The lead product candidates in our most advanced programs are aimed at druggable targets, which have undergone rigorous validation processes. Our most advanced cancer product candidates, AG-221 and AG-120, which target mutant isocitrate dehydrogenase 2 and 1, or IDH2 and IDH1, respectively. These mutations have been found in a wide range of hematological malignancies and solid tumors. The lead candidate in our rare genetic disorders program, AG-348, targets pyruvate kinase for the treatment of pyruvate kinase deficiency. Pyruvate kinase deficiency is a rare and often severe hemolytic anemia. All of our product candidates are in various stages of early clinical development.

Table of Contents

We are leveraging our expertise in metabolic pathways to discover, validate, develop and potentially commercialize a pipeline of novel drug candidates with a focus in cancer and rare genetic disorders of metabolism. In April 2010, and subsequently amended in October 2011 and July 2014, we entered into a collaboration agreement with Celgene Corporation, or Celgene, focused specifically on cancer metabolism. Under the collaboration, we are leading discovery, preclinical and early clinical development for all cancer metabolism programs. The discovery phase of the collaboration expires in April 2015, subject to Celgene s option to extend the discovery phase for up to one additional year.

Celgene has the option to obtain exclusive rights for the further development and commercialization of certain of these programs, and we will retain rights to the others. For the programs that Celgene chooses to license, we may elect to participate in a portion of sales and other commercialization activities for the medicines from such programs in the United States. In addition, for certain of these programs, we may elect to retain full rights to develop and commercialize medicines from these programs in the United States. In January 2014, we elected to exercise our option to retain development and commercialization rights to AG-120 in the United States. In June 2014, Celgene elected to exercise its option to an exclusive global license for development and commercialization of AG-221. Through September 30, 2014, we have received approximately $161.2 million in payments from Celgene and $62.7 million in equity investments under our agreements with Celgene. We are also eligible to receive an additional extension payment, if Celgene opts to extend the discovery phase, payments upon the successful achievement of specified milestones, reimbursements for certain development expenses and royalties on any product sales.

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 clinical trials. To date, we have financed our operations primarily through funding received from our collaboration agreement with Celgene, private placements of our preferred stock, the initial public offering, or IPO, of our common stock and concurrent private placement of common stock to an affiliate of Celgene and our follow-on public offering. Substantially all of our revenue to date has been collaboration revenue. In connection with the IPO, our Board of Directors and stockholders approved a 1-for-2.75 reverse stock split of our common stock. The reverse stock split became effective on July 11, 2013. All share and per share amounts in the consolidated financial statements have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital.

Since inception, we have incurred significant operating losses. Our net losses were $26.8 million and $27.0 million for the nine months ended September 30, 2014 and 2013, respectively. As of September 30, 2014, we had an accumulated deficit of $140.3 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 transition from IND-enabling studies to clinical development activities for our lead programs AG-221, AG-120, and AG-348; continue to discover and validate novel targets and drug product candidates; expand and protect our intellectual property portfolio; hire additional commercial, development and scientific personnel; and continue to operate as a publicly-traded company.

Table of Contents

**Financial Operations Overview**

***Revenue***

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales in the near future. All of our revenue to date has been derived from our collaboration with Celgene and funding from research grant agreements. Through the date of the amendment of our collaboration agreement in July 2014, we were recognizing revenue related to the upfront license fee of $121.2 million, the implied premium of $3.1 million paid on the purchase of $8.8 million of Series B Convertible Preferred Stock, and the two $20.0 million extension payments received in October 2011 and May 2014 to extend the discovery phase until April 2015, ratably over the period over which we expected to fulfill our performance obligations, which we referred to as the performance period. As a result of the amendment, we were required to reevaluate the agreement under the current revenue recognition accounting guidance. Under this guidance, the best estimate of selling price of all undelivered units of accounting was estimated and was determined to be less than the combination of future contractual consideration to be received and the remaining deferred revenue balance at the amendment date. As a result, we immediately recognized revenue on the amendment date related to the excess of total consideration over the best estimate of selling price of undelivered elements. For the period January 1, 2014 through the amendment date, we recognized a total of $42.7 million in revenues under the previous accounting guidance and upon the modification. We recognized $8.0 million in revenues related to the units of accounting subsequent to the modification date. We recognized total revenues of $33.9 million and $50.7 million in connection with the Celgene collaboration during the three and nine months ended September 30, 2014 respectively.

We will receive additional consideration under our collaboration agreement with Celgene related to certain development services to be performed. We may also be eligible to receive an additional $20.0 million extension payment in the event Celgene elects to extend the discovery phase until April 2016. We may also receive future milestone or royalty payments under the Celgene collaboration agreement. We expect that any revenue we generate from our collaboration agreement will fluctuate from quarter to quarter as a result of our analysis of each unit of accounting, primarily from the timing of revenue recognition related to the delivery of the license for AG-120, and the uncertain timing and amount of milestone payments, royalties and other payments.

In the future, we will seek to generate revenue from a combination of product sales and upfront payments, extension payments, cost reimbursements, milestone payments, and royalties on future product sales in connection with our Celgene collaboration or other strategic relationships.

***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.

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 AML. Based on our established preclinically-based target profiling, as well as preclinical *in vitro* and *in vivo* efficacy data and early clinical data, there is a clear rationale to develop AG-221 in defined target populations that harbor an IDH2 mutation.

We have conducted exploratory pharmacology studies to develop a model of IDH2 mutant-induced tumorigenesis and to characterize the binding, inhibition, and selectivity of AG-221. We have demonstrated in *in vitro* experiments and in *in vivo* models that exposure to AG-221 reduces the oncometabolite 2-hydroxyglutarate (2HG) levels to those found in normal cells and reverses 2HG-induced histone hypermethylation. Targeted inhibition of the IDH2 mutant also reversed the differentiation block in both TF-1 leukemia cells and primary AML cells derived from patients, thereby promoting normal differentiation to cells along the erythroid and myeloid lineage, respectively. During 2013, we successfully completed IND-enabling studies on AG-221. The molecule has excellent pharmacological properties with a wide therapeutic index.

Table of Contents

In September 2013, we initiated our first phase 1 study for AG-221 in patients with advanced hematologic malignancies with an IDH2 mutation. In October 2014, we initiated four expansion cohorts in our ongoing phase 1 study of AG-221 in patients with IDH2-mutant 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 hematologic malignancies, including AML. The expansion cohorts will evaluate 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 October 2014, we announced the initiation of a phase 1/2 multicenter study of AG-221 in patients with advanced solid tumors, including gliomas, as well as angioimmunoblastic T-cell lymphoma (AITL), in each case, that carry an IDH2 mutation. This phase 1/2 multicenter, open-label, dose-escalation clinical trial of AG-221, which is being conducted by Agios, is designed to assess the safety, clinical activity, and tolerability of AG-221 among patients who have an IDH2-mutant advanced solid tumor. The phase 1/2 trial is expected to include a dose expansion phase where three cohorts of patients with glioma, AITL and other solid tumors that are IDH2 mutant-positive will receive AG-221 to further evaluate safety, tolerability and clinical activity in advanced solid tumors.

In April 2014, we reported initial findings from the first two cohorts of patients treated with AG-221. The initial data were presented during a symposium titled Novel Immune and Targeted Therapies for Hematological Malignancies and Solid Tumors at the AACR Annual Meeting 2014. As of March 20, 2014, a total of 22 patients with relapsed or refractory AML, which means that disease had progressed after or was refractory to between one and four prior therapies, were treated with either 30 mg or 50 mg of AG-221 orally twice daily. At the time of data submission to the AACR Annual Meeting 2014, seven of 10 patients were evaluable for efficacy as they had completed the first 28 day cycle of therapy. Within the first dose cohort at the 30 mg twice-daily dose, three patients did not complete a full 28-day cycle of therapy and died due to complications of disease-related infection common in patients with relapsed or refractory AML. Of the seven evaluable patients, six patients had investigator-assessed objective responses, including three patients who achieved complete remission (CR), two patients who achieved complete remission with incomplete platelet recovery (CRp) and one patient with a partial response (PR). A complete remission 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 complete remission with incomplete platelet recovery 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 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 are decreased by at least 50% over pretreatment. One patient with a CR elected to be removed from the study to undergo a bone marrow transplant; all other patients with objective responses continued to receive the drug.

On June 14, 2014, we announced additional clinical data from the phase 1 study of AG-221, which included 35 patients with IDH2 mutant positive advanced hematologic malignancies. These data confirmed and built upon previously presented data on AG-221 s clinical activity, safety profile and unique mechanism of action. The data were presented at the 19th Congress of the European Hematology Association in Milan, Italy. The new data showed investigator-assessed objective responses in 14 out of 25 evaluable patients on AG-221 and an additional five patients with stable disease. In six patients who achieved a complete remission, evidence of durability was observed, ranging from one to four months in duration. AG-221 continued to show favorable drug exposure and pharmacokinetics at all doses tested with substantial reductions in plasma levels of 2HG. There were no discontinuations of AG-221 due to adverse events. The maximum tolerated dose had not yet been reached and the dose escalation continued. On October 15, 2014, we announced our plan to present additional clinical data from the ongoing AG-221 phase 1 study in advanced hematologic malignancies at the 2014 American Society of Hematology Annual Meeting.

On June 16, 2014, the U.S. Food and Drug Administration (FDA) granted us orphan drug designation for AG-221 for treatment of patients with AML. On August 13, 2014, we announced that the U.S. FDA granted Fast Track

designation to AG-221 for treatment of patients with AML that harbor an IDH2 mutation.

AG-221 s mechanism of response observed to date is consistent with preclinical studies, including substantial reduction of plasma 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 June 2014, Celgene exercised its option to an exclusive global license for development and commercialization of AG-221. Under the collaboration agreement, Celgene is responsible for all development costs for AG-221. We are eligible to receive up to $120 million in milestone payments and a tiered royalty on any net sales of products containing AG-221. 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 early clinical development and regulatory activities within the AG-221 development program in collaboration with Celgene. Celgene is responsible for all development costs for AG-221.

Table of Contents

***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. Importantly, mutations in IDH1 have been identified in difficult to treat cancers such as chondrosarcoma and cholangiocarcinoma where both the treatment options and prognosis for patients are poor. These are examples of indications where the standard of care treatment options are limited, thus providing an opportunity for more rapid development of an IDH1 mutant inhibitor. Based on our preclinical *in vitro* and *in vivo* efficacy data, there is a clear rationale to develop AG-120 in defined target populations that harbor an IDH1 gene mutation. We successfully filed an IND for AG-120 that was accepted by the FDA. The molecule has excellent pharmacological properties with a wide therapeutic index. In March 2014, we initiated two phase 1 studies for AG-120, one in patients with advanced hematologic malignancies and the second in patients with advanced solid tumors; both trials will only enroll patients that carry an IDH1 mutation. We plan to present clinical data from the ongoing AG-120 phase 1 study in advanced hematologic malignancies at the 26th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics on November 19, 2014 in Barcelona, Spain.

Celgene has the exclusive option to license development and commercialization rights to AG-120 outside the United States and, in January 2014, we elected to exercise our option to retain development and commercialization rights to AG-120 in the U.S. If Celgene exercises its option, we and Celgene will equally fund the global development costs of AG-120 that are not specific to any particular region or country, Celgene will be responsible for development and commercialization costs specific to countries outside the United States, and we will be responsible for development and commercialization costs specific to the United States.

***AG-348: Pyruvate Kinase (PK) Deficiency Program***

AG-348 is an orally available small molecule and a potent activator of the PKR enzyme, an isoform of PK that when mutated leads to PK deficiency, a rare and often severe hemolytic anemia. Preclinical *in vitro* data demonstrate that these activators can significantly enhance the activity and/or the stability of the majority of the common PKR mutants. This degree of enzyme activation leads to a meaningful correction of the metabolic imbalance normally found within mutant cells. Red blood cells have been obtained from patients with severe and moderate PK deficiency where ex vivo studies have demonstrated enzyme activation and metabolic improvement. We successfully completed IND-enabling studies and filed an IND for AG-348 that was accepted by the FDA. The molecule has excellent pharmacological properties with a projected wide therapeutic index. We initiated a single ascending dose (SAD)-escalation phase 1 clinical trial for AG-348 in healthy volunteers in April 2014 and initiated a multiple ascending dose (MAD)-escalation phase 1 clinical trial for healthy volunteers in June 2014. The SAD trial is complete and has met its primary endpoint. The MAD trial, while still ongoing, has also met its primary endpoint. The primary endpoint is defined in the protocol to identify a safe and pharmacodynamically active dose and schedule for AG-348 to be used in subsequent clinical studies in patients with pyruvate kinase deficiency. We plan to present clinical data from the ongoing AG-348 phase 1 study at the 2014 American Society of Hematology Annual Meeting.

We believe the clinical and regulatory strategy for our PK deficiency program has well-established primary and secondary endpoints similar to that of other approved medicines developed for the treatment of other anemias.

We have retained worldwide development and commercial rights to AG-348 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, lead optimization for our earlier validated and follow-on programs and our proprietary metabolomics platform.

Table of Contents

We track our internal and external research and development costs on a program-by-program basis. 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, to each of these programs based on the personnel resources allocated to such program. Our research and development expenses, by major program for the three and nine months ended September 30, 2014 and 2013, are outlined in the table below:

| | Three Months Ended September 30, | | Nine Months Ended September 30, | |
|---|---|---|---|---|
| **(in thousands)** | **2014** | **2013** | **2014** | **2013** |
| IDH2 (AG-221) | $ 5,632 | $ 2,128 | $ 15,039 | $ 7,734 |
| IDH1 (AG-120) | 5,690 | 2,958 | 14,222 | 8,270 |
| PK deficiency (AG-348) | 3,801 | 2,302 | 10,789 | 4,920 |
| Other research and platform programs | 10,403 | 7,415 | 25,459 | 18,299 |
| Total research and development expenses | $ 25,526 | $ 14,803 | $ 65,509 | $ 39,223 |

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-348, 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-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.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, potential commercialization of our product candidates and increased costs of operating as a public company. 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. Additionally, we anticipate increased costs associated with being a public company including expenses related to services associated with maintaining compliance with exchange listing and Securities and Exchange Commission requirements, insurance, and investor relations costs.

Table of Contents

**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, income taxes, accrued research and development expenses and stock-based compensation. In July 2014, we amended our collaboration agreement with Celgene. As a result of our conclusion that the arrangement was materially modified, we are required to apply the provisions of ASU No. 2009-13, *Multiple-Element Revenue Arrangements*, and will recognize revenue under this guidance on a prospective basis.

There have been no other significant changes to our critical accounting policies discussed in the Annual Report on Form 10-K for the year ended December 31, 2013.

**Results of Operations**

***Comparison of Three Months Ended September 30, 2014 and 2013***

The following table summarizes our results of operations for the three months ended September 30, 2014 and 2013, together with the changes in those items in dollars and as a percentage:

| | Three Months Ended September 30, | | | |
|---|---|---|---|---|
| **(in thousands)** | **2014** | **2013** | **Dollar Change** | **% Change** |
| Total revenue | $ 33,900 | $ 6,268 | $ 27,632 | 441% |
| Operating expenses: | | | | |
| Research and development | 25,526 | 14,803 | 10,723 | 72 |
| General and administrative | 5,166 | 2,534 | 2,632 | 104 |
| Income (loss) from operations | 3,208 | (11,069) | 14,277 | (129) |
| Interest income | 48 | 13 | 35 | 269 |
| Provision (benefit) for income taxes | (448) | 121 | (569) | (470) |
| Net income (loss) | $ 3,704 | $ (11,177) | $ 14,881 | (133)% |

*Revenue.* Revenue increased by $27.6 million to $33.9 million for the three months ended September 30, 2014 from $6.3 million for the three months ended September 30, 2013, an increase of 441%. In July 2014, we amended our agreement with Celgene which resulted in the application of new accounting guidance to the agreement. Prior to the amendment, arrangement consideration was recognized ratably over the estimated period of performance. As a result of the amendment, we were required to reevaluate the agreement under the current revenue recognition accounting guidance. Under this guidance, the best estimate of selling price of all undelivered units of accounting was estimated and was determined to be less than the combination of future contractual consideration to be received and the remaining deferred revenue balance at the amendment date. As a result, we immediately recognized revenue on the amendment date related to the excess of total consideration over the best estimate of selling price of undelivered elements, which fundamentally relates to previously delivered elements under the agreement and includes the exclusive global license for development and commercialization of AG-221 and the reimbursement of on-going development costs related to AG-221 through the amendment date. For the three months ended September 30, 2014,

we recognized a total of $25.9 million in revenue under the previous accounting guidance and upon the modification. We recognized $8.0 million in revenue related to the units of accounting subsequent to the modification date.

*Research and development expense.* Research and development expense increased by $10.7 million to $25.5 million for the three months ended September 30, 2014 from $14.8 million for the three months ended September 30, 2013, an increase of 72%. The increase in research and development expenses was attributable to an increase of $8.1 million in external services and $2.6 million in internal expenses. The increase in external services for the three months ended September 30, 2014 was attributable to the following:

- approximately $3.0 million, $2.2 million and $1.7 million for external phase 1 clinical studies and manufacturing activities for our lead product candidates targeting IDH2, IDH1 and PK deficiency, respectively; and

- approximately $1.2 million of costs related to other early research and platform programs.

We incurred approximately $2.6 million of additional internal research and development expenses related to the following:

- an increase of $1.9 million in personnel costs related to an increase in our internal headcount of 21%, which includes an increase of $0.5 million in stock-based compensation expense; and

- approximately $0.6 million for facilities and other related expenses, and $0.1 million for research materials related to our expanded research efforts.

Table of Contents

*General and administrative expense.* General and administrative expenses increased by $2.6 million to $5.1 million for the three months ended September 30, 2014 from $2.5 million for the three months ended September 30, 2013, an increase of 104%. The increase in general and administrative expenses was primarily attributable to the following:

- an increase of $1.5 million in personnel costs related to an increase in our internal headcount by 27% which includes an increase of $1.2 million for stock-based compensation expense;
- an increase of $1.0 million in professional service costs and insurance costs; and
- an increase of $0.1 million in certain operating expenses, including consulting and facility costs.

*Interest income.* Interest income increased by $35,000 to $48,000 for the three months ended September 30, 2014 from $13,000 for the three months ended September 30, 2013, an increase of 269%. The increase is attributable to interest earned on the net proceeds from our IPO in July 2013 and the follow-on offering in April 2014.

*(Benefit) provision for income tax.* The (benefit) provision for income taxes increased by $0.6 million to a $0.5 million benefit for the three months ended September 30, 2014, from a $0.1 million provision for income taxes for the three months ended September 30, 2013. In January 2014, we paid $6.0 million as payment in full of our U.S. federal income tax liability related to the year ended December 31, 2011, including $1.5 million of interest and penalties accrued. The increase in our benefit for income taxes for the three months ended September 30, 2014 was attributable to an abatement received in August 2014 from the Internal Revenue Service of $0.5 million related to penalties previously paid. For the three months ended September 30, 2013, the provision for income taxes was primarily attributable to penalties and interest accrued for the non-payment of U.S. federal income taxes.

***Comparison of Nine Months ended September 30, 2014 and 2013***

The following table summarizes our results of operations for the nine months ended September 30, 2014 and 2013, together with the changes in those items in dollars and as a percentage:

| | Nine Months Ended September 30, | | | |
|---|---|---|---|---|
| **(in thousands)** | **2014** | **2013** | **Dollar Change** | **% Change** |
| Total revenue | $ 50,722 | $ 18,804 | $ 31,918 | 170% |
| Operating expenses: | | | | |
| Research and development | 65,509 | 39,223 | 26,286 | 67 |
| General and administrative | 12,619 | 6,222 | 6,397 | 103 |
| Loss from operations | (27,406) | (26,641) | (765) | 3 |
| Interest income | 118 | 26 | 92 | 354 |
| Provision (benefit) for income taxes | (448) | 410 | (858) | (209) |
| Net loss | $ (26,840) | $ (27,025) | $ 185 | (1)% |

*Revenue.* Revenue increased by $31.9 million to $50.7 million for the nine months ended September 30, 2014 from $18.8 million for the nine months ended September 30, 2013, an increase of 170%. In July 2014, we amended our agreement with Celgene which resulted in the application of new accounting guidance to the agreement. Prior to the amendment, arrangement consideration was recognized ratably over the estimated period of performance. As a result of the amendment, we were required to reevaluate the agreement under the current revenue recognition accounting guidance. Under this guidance, the best estimate of selling price of all undelivered units of accounting was estimated and determined to be less than the combination of future contractual consideration to be received and the remaining deferred revenue balance at the amendment date. As a result we immediately recognized revenues on the amendment date related to the excess of total consideration over the best estimate of selling price of undelivered elements, which fundamentally relates to previously delivered elements under the agreement which includes the exclusive global license for development and commercialization of AG-221 and on-going development costs related to AG-221 through the amendment date. For the period January 1, 2014 through the amendment date, we recognized a total of $42.7 million in revenue under the previous accounting guidance and upon the modification. We recognized $8.0 million in revenue related to the units of accounting subsequent to the modification date. We recognized total revenues of $50.7 million in connection with the Celgene collaboration during the nine months ended September 30, 2014.

Table of Contents

*Research and development expense.* Research and development expense increased by $26.3 million to $65.5 million for the nine months ended September 30, 2014 from $39.2 million for the nine months ended September 30, 2013, an increase of 67%. The increase in research and development expenses was attributable to an increase of $19.1 million in external services and $7.2 million in internal expenses. The increase in external services for the nine months ended September 30, 2014 was attributable to the following:

- approximately $9.0 million of external costs related to phase 1 clinical studies, IND-enabling preclinical studies and manufacturing activities for our lead product candidates targeting IDH1 and PK deficiency;
- approximately $6.5 million of external costs for phase 1 clinical studies and manufacturing activities for our lead product candidate targeting IDH2; and
- approximately $3.6 million of costs related to other early research and platform programs.

We incurred approximately $7.2 million of additional internal research and development expenses related to the following:

- an increase of $6.0 million in personnel costs related to an increase in our internal headcount by 21% which includes an increase of $2.5 million for stock-based compensation expense; and
- approximately $1.0 million for facilities and other related expenses, and $0.2 million for research materials related to our expanded research efforts.

*General and administrative expense.* General and administrative expenses increased by $6.4 million to $12.6 million for the nine months ended September 30, 2014 from $6.2 million for the nine months ended September 30, 2013, an increase of 103%. The increase in general and administrative expenses was primarily attributable to the following:

- an increase of $3.6 million in personnel costs related to an increase in our internal headcount by 27% which includes an increase of $2.4 million for stock-based compensation expense;
- an increase of $2.3 million in professional service costs and insurance costs related to being a public company; and
- an increase of $0.5 million in certain operating expenses, including travel and facility costs.

*Interest income.* Interest income increased $92,000 to $118,000 for the nine months ended September 30, 2014 from $26,000 for the nine months ended September 30, 2013, an increase of 354%. The increase is attributable to interest earned on the net proceeds from our IPO in July 2013 and the follow-on offering in April 2014.

*(Benefit) provision for income tax.* The (benefit) provision for income taxes increased by $0.9 million to a $0.5 million benefit for the nine months ended September 30, 2014, from a $0.4 million provision for income taxes for the nine months ended September 30, 2013. In January 2014, we paid $6.0 million as payment in full of our U.S. federal income tax liability related to the year ended December 31, 2011, including $1.5 million of interest and penalties accrued. The increase in our benefit for income taxes for the nine months ended September 30, 2014 was attributable to an abatement received in August 2014 from the Internal Revenue Service of $0.5 million related to penalties previously paid. For the nine months ended September 30, 2013, the provision for income taxes was primarily attributable to penalties and interest accrued for the non-payment of U.S. federal income taxes.

**Liquidity and Capital Resources**

***Sources of Liquidity***

On July 29, 2013, we closed the IPO of our common stock, which resulted in net proceeds of $111.0 million after deducting underwriting discounts, commissions, and expenses payable by us. Additionally, an affiliate of Celgene purchased shares of common stock in a separate private placement concurrent with the completion of the offering for aggregate proceeds of $12.8 million.

On April 29, 2014, we completed a public offering of 2,000,000 shares of our common stock at a public offering price of $44.00 per share, before underwriting commissions and discounts. We received net proceeds from this offering of $82.3 million, after deducting underwriting discounts, commissions and expenses payable by us. Celgene purchased 294,800 shares of our common stock in the offering. In addition, we granted the underwriters the right to purchase up to an additional 300,000 shares of our common stock which was exercised in May 2014 resulting in additional net proceeds to us of $12.4 million, after underwriting discounts and commissions paid by us.

Table of Contents

Since our inception, and through September 30, 2014, we have raised an aggregate of approximately $499.6 million to fund our operations, of which approximately $161.2 million was received through upfront and extension payments related to our collaboration agreement with Celgene, approximately $120.0 million was received from the issuance of preferred stock, $111.0 million was received from the IPO, after deducting underwriting discounts, commissions, and expenses, approximately $12.8 million was received from the concurrent private placement of common stock to an affiliate of Celgene, and $94.7 million was received through our follow-on offering after deducting underwriting discounts, commissions and expenses. As of September 30, 2014, we had $237.9 million in cash, cash equivalents and marketable securities.

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 reimbursement under our collaboration agreement with Celgene, including $18.7 million which was due as of September 30, 2014 and subsequently received in October 2014. 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 agreement is our only committed potential external source of funds.

***Cash Flows***

The following table provides information regarding our cash flows for the nine months ended September 30, 2014 and 2013:

| | Nine Months Ended, September 30, | |
|---|---|---|
| **(in thousands)** | **2014** | **2013** |
| Net cash used in operating activities | $ (51,578) | $ (42,783) |
| Net cash used in investing activities | (46,034) | (66,807) |
| Net cash provided by financing activities | 96,101 | 124,304 |
| Net increase (decrease) in cash and cash equivalents | $ (1,511) | $ 14,714 |

***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. Net cash used in operating activities was $51.6 million during the nine months ended September 30, 2014 compared to $42.8 million during the nine months ended September 30, 2013. The increase in cash used in operating activities was primarily attributable to increased operating expenses which primarily relates to increases in Clinical study costs due to advancements in our three lead programs and increased staffing needs due to the expanding operations. In addition, we made a $6.0 million payment for our U.S. federal income tax obligations in January 2014. Our net loss was significantly reduced by revenue recognized due to the modification of the collaboration agreement with Celgene, however, no cash was received during the period related to this activity.

***Net Cash Used in Investing Activities***

Net cash used in investing activities was $46.0 million during the nine months ended September 30, 2014 compared to cash used in investing activities of $66.8 million during the nine months ended September 30, 2013. The cash used in

investing activities for the nine months ended September 30, 2014 and 2013 was primarily the result of higher purchases of marketable securities than proceeds from maturities and sales of marketable securities.

Table of Contents

***Net Cash Provided by Financing Activities***

Net cash provided by financing activities was $96.1 million during the nine months ended September 30, 2014 compared to $124.3 million during the nine months ended September 30, 2013. The cash provided by financing activities for the nine months ended September 30, 2014 was primarily the result of the proceeds from the follow-on public offering, net of underwriting discounts, commissions and offering costs. The cash provided by financing activities for the nine months ended September 30, 2013 was primarily the result of proceeds from the initial public offering, net of underwriting discounts, commissions and expenses and proceeds from the private placement.

***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. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. 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, the $3.8 million in anticipated refundable income taxes, anticipated interest income and anticipated expense reimbursements under our collaboration agreement with Celgene will enable us to fund our operating expenses and capital expenditure requirements until at least mid-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 collaboration with Celgene;
- whether Celgene exercises its remaining option to extend the discovery phase under our collaboration agreement which would trigger an extension payment to us;
- 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 revenues, 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 revenues, 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 collaboration 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 nine months ended September 30, 2014, we entered into agreements in the normal course of business with contract research organizations 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 September 30, 2014 we are obligated to pay up to $29.2 million to these vendors.

***Operating Lease***

On September 15, 2014, we entered into an operating lease agreement for 74,498 square feet of office and laboratory space located at 88 Sidney Street, Cambridge, Massachusetts. We also entered into an agreement to terminate our existing lease under which we currently lease 38,536 square feet of office and laboratory space located at 38 Sidney Street, Cambridge, Massachusetts. The date on which we will become responsible for paying rent under the new lease, which we refer to as the commencement date, will be the earlier of May 15, 2015 or the date upon which we first begin conducting business at the new location. Our existing lease will terminate thirty days after the commencement date. The initial lease term will be for a period of seven years from the commencement date. At the end of the lease term, we have the option to extend the lease for two consecutive terms of five years at fair market rent at the time of the extension. The lease agreement includes rent escalation clauses, a tenant improvement allowance of $11.2 million and access to temporary space located at the premises for no cost. We gained physical access to the leased space in September 2014 and began to record rent expense on a straight-line basis over the effective term of the lease. We provided a standby letter of credit of $1.4 million as security for our obligations under the lease, which was issued in October 2014.

Future annual minimum lease payments due under the new and existing operating leases at December 31 of each year are as follows (in thousands):

| | |
|---|---|
| 2014 | $ 677 |
| 2015 | 3,538 |
| 2016 | 4,318 |
| 2017 | 4,405 |
| 2018 | 4,493 |
| Thereafter | 15,826 |
| | $ 33,257 |

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, 2013.

**Item 3. Quantitative and Qualitative Disclosures About Market Risk.**

We are exposed to market risk related to changes in interest rates. As of September 30, 2014 and December 31, 2013, we had cash, cash equivalents and marketable securities of $237.9 million and $193.9 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 contract with CROs that are located in Asia and Europe, which 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 September 30, 2014 and December 31, 2013, we had minimal or no liabilities denominated in foreign currencies.

Table of Contents

**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 September 30, 2014, 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 Securities Exchange Act of 1934, as amended, or 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 September 30, 2014 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-lookin statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. You should read this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from what we expect. The risks described are not the only risks facing our Company. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition and/or operating results. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. These risk factors restate and supersede the risk factors set forth under the heading Risk Factors in our Annual Report on Form 10-K for the quarter ended December 31, 2013.

**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 $39.4 million, $20.1 million and $23.7 million for the years ended December 31, 2013, 2012 and 2011, respectively, and $26.8 million for the nine months ended September 30, 2014. As of September 30, 2014, we had an accumulated deficit of $140.3 million. 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 offering and our collaboration with Celgene focused on cancer metabolism. We have devoted substantially all of our efforts to research and development. We are in early stages of clinical development 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, such as during the three months ended September 30, 2014, which was the result of the recognition of previously deferred collaboration revenue, we generally 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;

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;

maintain, expand and protect our intellectual property portfolio;

hire additional clinical, quality control and scientific personnel;

add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and

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 revenues that are

Table of Contents

significant or large enough to achieve profitability. We are currently only in early clinical testing stages for our 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 the 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. Furthermore, we will continue to incur increased costs associated with operating as a public company. 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 September 30, 2014, the $3.8 million in anticipated refundable income taxes, anticipated interest income and anticipated expense reimbursements under our collaboration agreement with Celgene, will fund our operating expenses and capital expenditure requirements until at least mid-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 collaboration with Celgene;
- whether Celgene exercises its option to extend the discovery phase under our collaboration with Celgene (which would trigger an extension payment to us);
- 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 revenues, 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 revenues, 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 collaboration with Celgene, which is limited in scope and duration. 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 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

Table of Contents

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.

***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 an early 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 early clinical studies of our product candidates. All of our product candidates are still in preclinical and early 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. 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.

In addition, as a new business, 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.

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

***Our approach to the discovery and development of product candidates that target cellular metabolism is largely unproven, and we do not know whether we will be able to develop any medicines of commercial value.***

Our scientific approach focuses on using our proprietary technology to identify key metabolic enzymes in cancer, rare genetic disorders, which we refer to as RGDs, of metabolism 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.

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 revenues in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

Table of Contents

***We depend heavily on the success of our most advanced product candidates. All of our product candidates are still in early 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 most advanced product candidates, AG-221 and AG-120 for the treatment of hematological and solid tumors and AG-348 for the treatment of PK deficiency. We initiated phase 1 studies for our most advanced product candidates, AG-221, AG-120 and AG-348. We have not commenced clinical trials for any of our other product candidates. Our ability to generate product revenues, 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 us and our collaborators. The success of our product candidates will depend on many factors, including the following:

- 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 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.

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, AG-221, AG-120 and AG-348, 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.***

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. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

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;

Table of Contents

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, or DSMB, 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.

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.

Product development costs will also increase if we or our collaborators experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize our product candidates, any of which may harm our business and results of operations.

***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 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;

Table of Contents

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.

Furthermore, we rely on 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.

***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 product candidates are still in early-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. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development 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 early stage testing for treating cancer, RGDs or other diseases have later been found to cause side effects that prevented further development of the compound.

***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 our collaboration agreement with Celgene, 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. 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.

***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

Table of Contents

States as medical devices and require separate regulatory approval prior to commercialization. Given our limited experience in developing diagnostics, we expect 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 we, Celgene or any third parties that we or Celgene engage to assist 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.

***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 revenues 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;

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 no 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;

Table of Contents

- 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 revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any medicines that we develop 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 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 market approval.

There are also a number of product candidates in preclinical 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 International AG, Pfizer, Inc., and Genzyme, a Sanofi company. There are also biotechnology companies of various size 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. and Raze Therapeutics. 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.

Table of Contents

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 early 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.

***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 regulations that govern marketing approvals, pricing and reimbursement for new medicines vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a medicine 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 our collaborators might obtain marketing approval for a medicine in a particular country, but then be subject to price regulations that delay our commercial launch of the medicine, possibly for lengthy time periods, and negatively impact the revenues we or our collaborators are able to generate from the sale of the medicine in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our and our collaborators ability to commercialize any medicines successfully also will depend in part on the extent to which reimbursement for these medicines and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any medicine that we or our collaborators commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we or our collaborators may not be able to successfully commercialize any product candidate for which we or they obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved medicines, and coverage may be more limited than the purposes for which the medicine is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any medicine will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the medicine and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost medicines and may be incorporated into existing payments for other services. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently

restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our or our collaborators inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved medicines that we or they develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize medicines and our overall financial condition.

***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;

Table of Contents

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; 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.

**Risks Related to Our Dependence on Third Parties**

***We depend on our collaboration 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 our collaboration with Celgene focused on cancer metabolism. 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 for additional payments upon Celgene s election to extend the term of the discovery phase and provides us with royalty-based revenue if certain product candidates are successfully commercialized. We cannot predict the success of the collaboration.

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 revenues from these arrangements will depend on our collaborators abilities to successfully perform the functions assigned to them in these arrangements.

Table of Contents

Collaborations involving our product candidates, including our collaboration 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 collaboration 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.

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, 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, or JRC, 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. For example, under our agreement with Celgene, 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.

A collaborator 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, Celgene has the first right to maintain or defend our intellectual property rights under our collaboration arrangement 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.

We may lose certain valuable rights under circumstances identified in our collaborations, including, in the case of our agreement 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 agreement with us, in its entirety or with respect to any program, upon 90 days notice and can terminate the 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.

Table of Contents

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 our collaboration with Celgene, 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 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.

***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 expect to rely on third parties, such as contract research organizations, or CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. 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, or EEA, 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

Table of Contents

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 revenues could be delayed.

We also expect 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 early 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 and AG-348 for our ongoing and planned phase 1 testing from third party manufacturers. We do not have a long term supply agreement with the third-party manufacturers, and we purchase our required drug supply on a purchase order basis.

We may be unable to establish any 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, and safety and pharmacovigilance reporting.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside the United States. 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.

Table of Contents

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 manufacturer 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. To date, we do not own or have any rights to issued patents that cover each of our most advanced product candidates, AG-221, AG-120, and AG-348, and we cannot be certain that we will secure rights to issued patents with claims that cover each of our proprietary medicines and technologies.

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.

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 which protect our technology or medicines or which 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 any 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

Table of Contents

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 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 collaborator may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or our collaborator 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.

Table of Contents

***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.

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

***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, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by

Table of Contents

comparable 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 regulatory 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.

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 revenues will be materially impaired.

***Failure to obtain marketing approval in international 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, it is required that the 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 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 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, 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. The FDA closely regulates the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes 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.

Table of Contents

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

- restrictions on such medicines, 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 clinical trials;
- warning or untitled letters;
- withdrawal of the medicines from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of medicines;
- 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; and
- injunctions or the imposition of civil or criminal penalties.

***Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which 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 play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and

customers 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 our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal healthcare 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 either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;

- the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- the federal transparency requirements under the Affordable Care Act requires manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and

- analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and 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 in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

Table of Contents

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, exclusion 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 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.

***Recently enacted and future legislation may increase the difficulty and cost for us or our collaborators to obtain marketing approval of and commercialize our 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 prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our or our collaborators ability to profitably sell any product candidates for which we or they obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

More recently, in March 2010, U.S. President Barack Obama signed into law the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Affordable Care Act revises the definition of average manufacturer price for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with health care practitioners. We will not know the full effects of the Affordable Care Act until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Affordable Care Act, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. 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 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 David Schenkein, M.D., our chief executive officer, J. Duncan Higgons, our chief operating officer, Scott Biller, Ph.D., our chief scientific officer, and Christopher Bowden, M.D., our chief medical officer, as well as the other principal members of our management and scientific teams. Drs. Schenkein, Biller and Bowden, and Mr. Higgons are 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 health-care 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.

**Risks Related to Our Common Stock**

***Our executive officers, directors and principal stockholders own a significant percentage of our stock and will be able to control matters submitted to stockholders for approval.***

As of November 6, 2014 our executive officers, directors and a small number of our stockholders own more than a majority of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to control 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, would control 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.

***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

Table of Contents

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. Any 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.

***The price of our common stock may be volatile and fluctuate substantially, 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. Since our initial public offering in July 2013 the price of our common stock on the NASDAQ Global Select Market has ranged from $15.77 per share to $88.82 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:

the success of competitive products or technologies;

results of clinical trials of our product candidates or those of our competitors;

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

Table of Contents

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 discover, develop, acquire or in-license additional product candidates or medicines;

actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

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

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.***

Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock. If such persons 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 could have a material adverse effect on the trading price of our common stock.

***Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our stock incentive plans, 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.

Pursuant to our stock incentive plan(s), our compensation committee (or its designee) and board of directors are authorized to grant equity-based incentive awards to our employees, directors and consultants. As of November 6, 2014, the number of shares of our common stock available for future grant under our 2013 Stock Incentive Plan, or the 2013 Plan, is 702,726.

The number of shares of our common stock reserved for issuance under our 2013 Plan will be increased (i) from time to time by the number of shares of our common stock forfeited upon the expiration, cancellation, forfeiture, cash settlement or other termination of awards under our 2007 Stock Incentive Plan, and (ii) 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 (x) 2,000,000 shares of our common stock, (y) 4% of the outstanding shares on such date or (z) an amount determined by our board of directors. Future option grants and issuances of common stock under our 2013 Plan may have an adverse effect on the market price of our common stock.

Table of Contents

***Commencing January 1, 2015, we will no longer be an emerging growth company, and the reduced disclosure requirements applicable to emerging growth companies will no longer apply to us.***

We are currently an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012. Because as of June 30, 2014, the market value of our common stock that was held by non-affiliates exceeded $700 million, we will no longer qualify for such status commencing January 1, 2015. As a large-accelerated filer, we will be subject to certain disclosure requirements that are applicable to other public companies that have not been applicable to us as an emerging growth company. These requirements include:

- compliance with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- compliance with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor s report providing additional information about the audit and the financial statements;
- full disclosure obligations regarding executive compensation; and
- compliance with the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

In addition, we will no longer be able to take advantage of transition periods for complying with new or revised accounting standards that are available to emerging growth companies.

***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 commencing January 1, 2015 when we will no longer be an emerging growth company, we do and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. 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. Our management and other personnel 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.

Commencing January 1, 2015, we will no longer be an emerging growth company and as such we will not be able to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are emerging growth companies as has been the case to date.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, commencing January 1, 2015, we will be required to furnish with our periodic Exchange Act reports a report by our management on our internal control over financial reporting. Commencing January 1, 2015, because we will no longer be an emerging growth company, we will be 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 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is 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, within the prescribed timeframe, or at all, 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.

***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.

Table of Contents

**Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.**

***Use of Proceeds***

On July 29, 2013, we completed our IPO in which we issued and sold 6,772,221 shares of our common stock, including 883,333 shares of common stock sold pursuant to the underwriters full exercise of their option to purchase additional shares, at a public offering price of $18.00 per share, for aggregate gross proceeds of $121.9 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-189216), which was declared effective by the SEC on July 23, 2013, and a Registration Statement on Form S-1 (File No. 333-190091) filed pursuant to Rule 462(b) of the Securities Act. J.P. Morgan Securities LLC and Goldman, Sachs & Co. acted as joint-book-running managers of the offering and as representatives of the underwriters. Cowen and Company, LLC and Leerink Swann LLC acted as co-managers for the offering. The offering commenced on July 23, 2013 and did not terminate until the sale of all of the shares offered. The net offering proceeds to us, after deducting underwriting discounts of $8.5 million and offering expenses payable by us totaling $2.4 million, were $111.0 million.

As of September 30, 2014, we have used approximately $97.6 million of the net offering proceeds primarily to fund the costs of phase 1 clinical development of AG-221, AG-120, and AG-348, to fund research and development to advance our pipeline of earlier-stage cancer metabolism and RGD programs and for working capital and general corporate purposes. None of the offering proceeds were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates. We are holding a significant portion of the balance of the net proceeds from the offering in money market funds and current- and non-current investments. Our use of the net offering proceeds to date is consistent with the use of proceeds described in our prospectus filed with the SEC pursuant to Rule 424(b)(4) on July 24, 2013, or the prospectus, and there has been no material change in our planned use of the balance of the net proceeds from the offering described in the prospectus.

**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: November 7, 2014 By: /s/ David P. Schenkein
**David P. Schenkein**

**Chief Executive Officer**

**(principal executive officer)**

Date: November 7, 2014 By: /s/ Glenn Goddard
**Glenn Goddard**

**Senior Vice President, Finance**

**(principal financial and accounting officer)**

Table of Contents

## EXHIBIT INDEX

| Exhibit Number | Description of Exhibit | Incorporated by Reference | | | | Filed Herewith |
|---|---|---|---|---|---|---|
| | | Form | File Number | Date of Filing | Exhibit Number | |
| 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 | Lease for 88 Sidney Street, dated September 15, 2014, by and between Agios Pharmaceuticals, Inc. and Forest City 88 Sidney, LLC | 8-K | 001-36014 | September 15, 2014 | 10.1 | |
| 10.2 | Termination of Lease, dated September 15, 2014, by and between Agios Pharmaceuticals, Inc. and 38 Sidney Street Limited Partnership | 8-K | 001-36014 | September 15, 2014 | 10.2 | |
| 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 |