AGIOS PHARMACEUTICALS INC
Form 424B5
December 11, 2014
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CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered[(1)]	Proposed maximum offering price per unit	Proposed maximum aggregate offering price[(1)]	Amount of registration fee[(2)]
Common Stock, par value $0.001 per share	2,284,423	$110.75	$252,999,847	$29,399

(1) Assumes exercise in full of the underwriters option to purchase up to 297,968 additional shares of Common Stock.

(2) Calculated in accordance with Rule 457(r) under the Securities Act of 1933, as amended. This Calculation of Registration Fee table shall be deemed to update the Calculation of Registration Fee table in the registrant s Registration Statement on Form S-3 (File No. 333-200822) in accordance with Rules 456(b) and 457(r) under the Securities Act of 1933, as amended.

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Filed in Pursuant to Rule 424(b)(5)
Registration No. 333-200822

Prospectus supplement

(To Prospectus dated December 9, 2014)

1,986,455 Shares

Common Stock

Agios Pharmaceuticals, Inc. is offering 1,986,455 shares of its common stock.

Our common stock is listed on The NASDAQ Global Select Market under the symbol AGIO. The last reported sale price of our common stock on The NASDAQ Global Select Market on December 10, 2014 was $111.55 per share.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012, and as such, have elected to comply with certain reduced public reporting requirements.

Investing in our common stock involves risks. See Risk factors beginning on page S-10 of this prospectus supplement, as well as those contained in the accompanying prospectus and the documents incorporated herein and therein.

	Per share	Total
Public offering price	$ 110.75	$ 219,999,891
Underwriting discounts(1)	$ 6.37	$ 12,649,994
Proceeds, before expenses, to Agios Pharmaceuticals, Inc.	$ 104.38	$ 207,349,897

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. See Underwriting beginning on page S-21 of this prospectus supplement.

We have granted the underwriters the right to purchase up to an additional 297,968 shares of our common stock at the public offering price less the underwriting discounts and commissions. The underwriters can exercise this right at any time within 30 days after the date of this prospectus supplement.

Celgene Corporation, or Celgene, an affiliate of two of our existing stockholders and our cancer metabolism strategic alliance partner, has indicated an interest in purchasing an aggregate of up to approximately 228,645 shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, Celgene may determine to purchase fewer shares than they have indicated an interest in purchasing or not to purchase any shares in this offering. In addition, the underwriters could determine to sell fewer shares to Celgene than Celgene indicated an interest in purchasing or not to sell any shares to Celgene. The underwriters will receive the same underwriting discount on any shares purchased by Celgene as they will on any other shares sold to the public in this offering. Any shares sold to Celgene will be subject to the lock-up agreements described under Underwriting.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to investors on or about December 16, 2014.

J.P. Morgan **Goldman, Sachs & Co.**

Cowen and Company **Leerink Partners**

The date of this prospectus supplement is December 10, 2014.

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PROSPECTUS SUPPLEMENT

PROSPECTUS

Neither we nor the underwriters have authorized anyone to provide you with information other than that contained in this prospectus supplement and the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and the underwriters take

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no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give to you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus is accurate only as of its date, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

No action is being taken in any jurisdiction outside the United States to permit a public offering of our common stock or possession or distribution of this prospectus supplement and the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement and the accompanying prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement and the accompanying prospectus applicable to that jurisdiction.

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About this prospectus supplement

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should rely only on the information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein. We have not authorized, and the underwriters have not authorized, anyone to provide you with information that is different. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled Where you can find more information and Incorporation of documents by reference in this prospectus supplement and in the accompanying prospectus.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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Prospectus supplement summary

This summary does not contain all of the information that you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the financial statements and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision. In addition, please read the Risk factors section of this prospectus supplement beginning on page S-10 and the risk factors contained in our Annual Report on Form 10-K for the year ended December 31, 2013 and our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2014, June 30, 2014 and September 30, 2014.

Overview

We are a biopharmaceutical company committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and rare genetic 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 focus our efforts on using cellular metabolism, an unexploited area of biological research with disruptive potential, as a platform for developing potentially transformative small molecule medicines. Our most advanced cancer product candidates, AG-221 and AG-120, 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-R for the treatment of pyruvate kinase deficiency. Pyruvate kinase deficiency is a rare disorder which often results in severe hemolytic anemia due to inherited mutations in the pyruvate kinase enzyme within red blood cells.

Targeting isocitrate dehydrogenase (IDH) for the treatment of cancer

The isocitrate dehydrogenase, or IDH, protein is a critical enzyme in the citric acid cycle, also known as the tricarboxylic acid, or Krebs, cycle. The Krebs cycle is centrally important to many biochemical pathways, and is one of the earliest established components of cellular metabolism. The Krebs cycle converts an essential cellular metabolite called isocitrate into another metabolite, alpha-ketoglutarate (a-ketoglutarate), both of which are critically important for cellular function and the creation of energy. In humans, there are three forms of the IDH enzyme, IDH1, IDH2, and IDH3, but only IDH1 and IDH2 appear to be mutated in cancers. IDH1 and IDH2 catalyze the same reaction but in different cellular compartments: IDH1 is found in the cytoplasm of the cell and IDH2 in the mitochondria. Tumor cells are generally observed to carry either an IDH1 or IDH2 mutation, but not both.

Using our proprietary metabolic platform, we and our collaborators examined the mutated pathway and discovered that the mutated IDH enzymes had adopted a novel gain of function activity that allows only the mutated IDH enzyme to produce large amounts of a metabolite called 2 hydroxygluturate, or 2HG. We believe that the excessive levels of the metabolite 2HG produced by the tumor fuel cancer growth and survival via multiple cellular changes that lead to a block in cell maturation, or differentiation. We believe that inhibition of these mutated proteins will lead to clinical benefit for the subset of cancer patients whose tumors carry these mutations. We have identified selective development candidates that target and inhibit the mutated forms of IDH1 and IDH2. To date our preclinical *in vitro* and *in vivo* efficacy data and early clinical data of AG-221 and AG-120, our lead inhibitors of mutant IDH2 and IDH1, respectively demonstrate a mechanism of response that 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.

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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. 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. We have been evaluating AG-221 in several phase 1b dose escalation trials evaluating both hematological and solid tumor cancers with IDH2 mutations. To date, all clinical data reported by us highlights that the mechanism of response 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. We intend to begin a global registration program for AG-221 in 2015 for IDH2-mutant positive hematologic malignancies.

In September 2013, we initiated our first phase 1 study for AG-221 in patients with advanced hematologic malignancies with an IDH2 mutation and in April 2014, we reported initial findings from the first two cohorts of patients treated with AG-221 at the American Association for Cancer Research (AACR) Annual Meeting 2014 in San Diego, California. As of March 20, 2014, a total of 22 patients with relapsed or refractory AML, which means that their 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. AG-221 demonstrated favorable drug exposure and pharmacokinetics with substantial reductions in plasma levels of 2HG. Preliminary analysis of pharmacokinetics at the 30 mg and 50 mg dose levels demonstrated excellent oral AG-221 exposure and a mean plasma half-life of greater than 40 hours. Given the long half-life observed, we announced that we intended to expand the trial to include once daily dosing cohorts, beginning with 100 mg.

On June 14, 2014, we presented additional clinical data from the phase 1 study of AG-221 at the 19th Congress of the European Hematology Association in Milan, Italy. These data built upon previously presented data on AG-221 s clinical activity, safety profile and unique mechanism of action and included 35 patients with IDH2-mutant positive advanced hematologic malignancies. 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. In June 2014, Celgene exercised its option to an exclusive global license for development and commercialization of AG-221.

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

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dose in approximately 100 patients with IDH2-mutant hematologic malignancies, including AML. The expansion cohorts are evaluating 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.

On December 7, 2014, we reported additional clinical data from the phase 1 study of AG-221, which included 73 enrolled patients with IDH2-mutant positive advanced hematologic malignancies. The data were presented at the 56th Annual Meeting of the American Society of Hematology (ASH) Annual Meeting and Exposition in San Francisco, California. The new data showed investigator-assessed objective responses in 25 out of 45 evaluable patients on AG-221. Of the 25 patients who achieved an objective response, there were six complete remissions, four complete remissions with incomplete platelet recovery (CRp), four marrow complete remissions (mCR), one complete remission with incomplete hematologic recovery (CRi) and ten partial remissions (PR). In the six patients who achieved a complete remission, evidence of durability was observed as long as eight months in duration and there have been no relapses in these patients. An estimated 90 percent of responses are three months or longer, with four responders on AG-221 beyond six months of treatment. Ten patients with stable disease remain on AG-221, with several patients on study as long as six months and ongoing. Five patients were removed from the study per the protocol following decision to undergo a potentially curative bone marrow transplant. 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. In addition, on December 7, 2014, we announced our intention to initiate a global registration program for AG-221 in 2015 as well as to initiate combination trials of AG-221 for the treatment of frontline hematological malignancies.

AG-120: lead IDH1 program

AG-120 is an orally available, selective, potent inhibitor of the mutated IDH1 protein, making it a highly targeted therapeutic candidate for the treatment of patients with cancers that harbor IDH1 mutations. Mutations in IDH1 have been identified in difficult to treat liquid and solid tumor cancers, including AML, chondrosarcoma and cholangiocarcinoma where both the treatment options and prognosis for patients are poor. In March 2014, we initiated two phase 1 studies for AG-120, one in patients with advanced hematologic malignancies and the second in patients with advanced solid tumors; both trials are only enrolling patients that carry an IDH1 mutation.

In November 2014, we reported initial 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. As of October 17, 2014, a total of 17 patients with a documented IDH1 mutation whose cancer relapsed or were refractory, meaning they failed to respond to at least one prior treatment regimen were treated with AG-120. At the time of the data cut, 14 patients with relapsed and/or refractory AML were evaluable; three patients recently initiated therapy and were not evaluable. The initial data showed investigator-assessed objective responses in seven out of 14 evaluable patients, including four complete remissions, with responses observed across the four dose levels tested. In the four patients who achieved a complete remission, durability ranging from 15 days to five months was observed. All responding patients remain on AG-120. One patient with stable disease remains on AG-120. AG-120 was well

tolerated, with the majority of adverse events reported as mild to

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moderate. The maximum tolerated dose has not yet been reached. One patient had a dose limiting toxicity of asymptomatic grade 3 QT prolongation at the highest dose tested to date, which improved to grade 1 after AG-120 dose reduction according to treatment protocol. This patient is in complete remission and remains on AG-120. AG-120 showed favorable drug exposure and pharmacokinetics at all doses tested and also substantially reduced plasma levels of the oncometabolite 2-hydroxyglutarate (2HG), which is produced by the mutant IDH1 protein, to the level observed in healthy volunteers. The mechanism of response is consistent with differentiation, as evidenced by the maturation of the leukemic cells into infection fighting white blood cells, or neutrophils. Based on these findings, we plan to initiate multiple expansion cohorts in the first half of 2015. We intend to initiate a global registration program for AG-120 in IDH1-mutant positive hematologic malignancies by early 2016.

AG-348: pyruvate kinase (PK) deficiency program

PK deficiency, a rare genetic disorder, manifests by mild to severe forms of anemia caused by the excessive premature destruction of red blood cells. The inherited mutations in PKR enzymes cause a deficit in cellular energy within the red blood cell, as evidenced by a build-up of the metabolite 2,3-DPG (2,3-diphosphoglycerate) and a decline in the energy metabolite ATP (adenosine triphosphate).

We are developing AG-348 as an orally available small molecule and a potent activator of the pyruvate kinase-R, or PKR, enzyme, an isoform of PK that when mutated leads to PK deficiency. Agios scientists have previously reported that AG-348 is a potent activator of the wild-type and mutated PKR enzymes, resulting in restoration of ATP levels and a decrease in 2,3-DPG levels in blood sampled from patients with PK deficiency. The wild-type PKR activity of AG-348 allows the study of enzyme activation in healthy volunteers, providing an opportunity to understand the safety, dosing and pharmacodynamic activity of AG-348 prior to entering a proof-of-concept study in patients.

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

On December 8, 2014, during a poster session at ASH 2014, we reported first clinical data from the phase 1 SAD and MAD clinical trials of AG-348 in healthy volunteers. These results provided early proof-of-mechanism for AG-348 as a novel, first-in-class, oral activator of both wild-type (normal) and mutated PKR enzymes. In these phase 1 studies, dosing of AG-348 over 14-days in healthy volunteers resulted in a dose-dependent increase in the PKR pathway as evidenced by a substantial increase in ATP and decrease in 2,3-DPG levels, which are key biomarkers of PKR activity and primary indicators of PK deficiency. These data support the hypothesis that AG-348 treatment may similarly enhance PKR activity in patients with PK deficiency and thus correct the underlying defect of the disease. Results presented are from 64 healthy volunteers who received either AG-348 or placebo, which includes 48 people from the completed SAD study and 16 people in the first two cohorts of the ongoing MAD study that recently completed enrollment. Complete safety results are being reported from the SAD phase 1 study and showed that AG-348 was well tolerated. Although the MAD study remains blinded, no serious adverse events have been reported in the first two analyzed cohorts. AG-348 also showed a favorable pharmacokinetic profile with rapid absorption, low variability and dose-proportional increase in exposure following both single and multiple doses. The observed dose-dependent changes in 2,3-DPG and ATP blood levels seen are consistent with a substantial increase in PKR enzymatic activity. We expect to provide final results from the MAD study in 2015 and to initiate a phase 2 study of AG-348 in patients with PK deficiency in the first half of 2015. A natural history study of PK deficiency is also ongoing and patient enrollment is on track.

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Collaboration with Celgene

In April 2010, we entered into a discovery and development collaboration and license agreement with Celgene, focused on targeting cancer metabolism. The goal of the collaboration is to discover, develop and commercialize disease-altering therapies in oncology arising out of our cancer metabolism research platform that have achieved development candidate status. On December 8, 2014, Celgene elected to extend the period of its exclusivity for an additional year to April 2016. The extension marks the final year for the discovery phase and Celgene will maintain its exclusive option to drug candidates that emerge from our cancer metabolism research platform through April 2016. We will receive a $20 million payment as a result of the extension.

Following this extension, the discovery portion of the collaboration will expire on April 14, 2016. Under the terms of the original agreement, we lead research, preclinical and early development efforts through phase 1, while Celgene receives an option to obtain exclusive rights either upon IND acceptance or at the end of phase 1, to further development and commercialize medicines emerging from our cancer metabolism research. Celgene would lead and fund global development and commercialization of some of these drugs, and we would retain development and commercialization rights for certain drugs in the U.S. On all programs, we are eligible to receive up to $120 million in milestone-based payments as well as royalties on any sales.

AG-221 and AG-120 are two drug candidates that have been nominated to date during the discovery phase of the collaboration. In June 2014, Celgene exercised its exclusive option to license AG-221 and gained worldwide development and commercialization rights for AG-221. We continue to conduct early clinical development activities within the AG-221 development program. We are also collaborating with Celgene on the development of AG-120. We retain U.S. development and commercialization rights for AG-120, and Celgene has an exclusive option to the ex-U.S. rights.

Our strategy

We aim to build a multi-product company, based on our expertise in cellular metabolism, that discovers, develops and commercializes first- and best-in-class medicines to treat cancer and rare genetic disorders. Key elements of our strategy include:

- Aggressively pursuing the development of novel medicines to transform the lives of patients with cancer and rare genetic disorders.

- Maintaining our competitive advantage and singular focus in the field of cellular metabolism.

- Continuing to build a product engine for cancer and rare genetic disorders to generate novel and important medicines.

- Building a preeminent independent biopharmaceutical company by engaging in discovery, development and commercialization of our medicines.

Maintaining a commitment to precision medicine in drug development.

Our guiding principles

We aim to build a long-term company with a disciplined focus on developing medicines that transform the lives of patients with cancer and rare genetic disorders. We maintain a culture of high integrity that embraces the following guiding principles, which we believe will provide long-term benefits for all our stakeholders:

Follow the science and do what is right for patients.

Maintain a culture of incisive decision-making driven by deep scientific interrogation and respectful irreverence.

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Foster collaborative spirit that includes all employees regardless of function or level.

Leverage deep strategic relationships with our academic and commercial partners to improve the quality of our discovery and development efforts.

Risks associated with our business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the Risk factors section of this prospectus supplement immediately following this prospectus supplement summary. These risks include the following:

We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability. As of September 30, 2014, we had an accumulated deficit of $140.3 million.

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.

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.

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

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

We 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.

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. We currently have patent protection for one of our lead product candidates in the United States, and do not own or license any issued patents for our other lead product candidates in major markets such as the United States and Europe.

If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we 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 corporate information

We were incorporated under the laws of the State of Delaware in August 2007. Our executive offices are located at 38 Sidney Street, 2nd Floor, Cambridge, Massachusetts 02139, and our telephone number is (617) 649-8600. Our website address is www.agios.com. The information contained in, or accessible through, our website does not constitute part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

As used in this prospectus supplement, unless the context otherwise requires, references to Agios, we, us, our and similar references refer to Agios Pharmaceuticals, Inc. and, where appropriate, our consolidated subsidiary. The trademarks, trade names and service marks appearing in this prospectus supplement are the property of their respective owners.

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The offering

Common stock offered	1,986,455 shares
Common stock to be outstanding after this offering	36,628,994 shares
Option to purchase additional shares	The underwriters have an option for a period of 30 days to purchase up to 297,968 additional shares of our common stock.
Use of proceeds	We intend to use the net proceeds from this offering as follows: approximately $70-100 million to fund the costs of phase 1 clinical development of AG-120, and initiating a global registration program; approximately $20-30 million to fund the phase 1/2 clinical development activities for AG-348; approximately $50-70 million to fund research and development to advance our pipeline of earlier-stage cancer metabolism and rare genetic disorders programs; and the remainder for working capital and other general corporate purposes. See Use of proceeds for more information.
Risk factors	See Risk factors beginning on page S-10 and the other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus for a discussion of certain factors you should carefully consider before deciding to invest in shares of our common stock.
The NASDAQ Global Select Market symbol	AGIO

The number of shares of our common stock to be outstanding after this offering is based on 34,642,539 shares of our common stock outstanding as of September 30, 2014.

The number of shares of our common stock to be outstanding after this offering excludes:

- 3,816,834 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2014 at a weighted-average exercise price of $13.74 per share;
- 799,270 shares of common stock reserved as of September 30, 2014 for future issuance under our equity incentive plans; and
- 327,272 shares of common stock reserved as of September 30, 2014 for future issuance under our 2013 employee stock purchase plan.

Unless otherwise indicated, this prospectus supplement reflects and assumes the following:

- no exercise of the outstanding options described above; and
- no exercise by the underwriters of their option to purchase additional shares.

Celgene Corporation, or Celgene, an affiliate of two of our existing stockholders and our cancer metabolism strategic alliance partner, has indicated an interest in purchasing an aggregate of up to approximately 228,645 shares of our common stock in this offering at the public offering price. However, because indications of interest are not binding agreements or commitments to purchase, Celgene may determine to purchase fewer shares than they have indicated an interest in purchasing or not to purchase any shares in this offering. In addition, the underwriters could determine to sell fewer shares to Celgene than Celgene indicated an interest in purchasing or not to sell any shares to Celgene. Any shares sold to Celgene will be subject to the lock-up agreements described under Underwriting.

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Summary consolidated financial data

The following table summarizes our consolidated financial data. We have derived the following summary of our consolidated statement of operations data for the nine months ended September 30, 2014 and the consolidated balance sheet data as of September 30, 2014 from our unaudited condensed consolidated financial statements incorporated by reference in this prospectus supplement from our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2014. We derived the consolidated statement of operations data for the years ended December 31, 2013, 2012 and 2011 from our audited consolidated financial statements incorporated by reference in this prospectus supplement from our Annual Report on Form 10-K for the year ended December 31, 2013. You should read this data together with our audited consolidated financial statements and related notes and the information under the captions Selected Consolidated Financial Data and Management s Discussion and Analysis of Financial Condition and Results of Operations, which are included in our Annual Report on Form 10-K for the year ended December 31, 2013 and our unaudited Quarterly Report on Form 10-Q for the nine months ended September 30, 2014 and incorporated by reference in this prospectus supplement. For more details on how you can obtain the documents incorporated by reference in this prospectus supplement, see Where you can find more information and Incorporation of documents by reference appearing elsewhere in this prospectus supplement. Our historical results are not necessarily indicative of future results.

(in thousands, except share and per share amounts)	Nine months ended September 30, 2014	Year Ended December 31, 2013	2012	2011
Consolidated statement of operations data:				
Revenue related party	$ 50,722	$ 25,548	$ 25,106	$ 21,837
Operating expenses:				
Research and development	65,509	54,502	41,037	31,253
General and administrative	12,619	9,929	7,064	7,215
Total operating expenses	78,128	64,431	48,101	38,468
Loss from operations	(27,406)	(38,883)	(22,995)	(16,631)
Interest income	118	55	69	132
Loss before provision (benefit) for income taxes	(27,288)	(38,828)	(22,926)	(16,499)
Provision (benefit) for income taxes	(448)	579	(2,824)	7,207
Net loss	(26,840)	(39,407)	(20,102)	(23,706)
Cumulative preferred stock dividends		(4,162)	(7,190)	(3,100)
Net loss applicable to common stockholders	$ (26,840)	$ (43,569)	$ (27,292)	$ (26,806)

Net loss per share applicable to common stockholders basic and diluted	$ (0.81)	$ (2.83)	$ (8.02)	$ (8.90)
Weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted	33,176,801	15,415,373	3,401,719	3,013,366

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(in thousands)	As of September 30, 2014 Actual	As Adjusted(1)
Consolidated balance sheet data:		
Cash, cash equivalents and marketable securities	$ 237,887	$ 444,637
Total assets	269,608	476,358
Total liabilities	61,859	61,859
Common stock	35	37
Additional paid-in capital	347,947	554,695
Accumulated deficit	(140,284)	(140,284)
Total stockholders equity	207,749	414,499

(1) The as adjusted consolidated balance sheet data gives effect to the issuance and sale of shares of our common stock in this offering at the public offering price of $110.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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Risk factors

An investment in our common stock involves risks. You should carefully consider the following risk factors, as well as the risk factors included in our Annual Report on Form 10-K for the year ended December 31, 2013 and our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2014, June 30, 2014 and September 30, 2014, together with all of the other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus in evaluating an investment in our common stock. If any of the following risks were to occur, our business, financial condition or results of operations could be materially adversely affected. In that case, the trading price of our common stock could decline and you could lose all or part of your investment.

Risks related to our common stock and this offering

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

Upon completion of this offering, our executive officers, directors and a small number of our stockholders will continue to 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 you may desire.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after giving effect to this offering. If you purchase common stock in this offering, you will incur an immediate and substantial dilution in net tangible book value of $99.43 per share, after giving effect to the sale by us of shares in this offering at the public offering price of $110.75 per share. In the past, we have issued options to acquire common stock at prices significantly below this offering price. To the extent these outstanding options are ultimately exercised, you will incur additional dilution.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses, and these financial losses could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

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

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 your sole source of gain for the foreseeable future.

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Cautionary note regarding forward-looking statements

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, 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, project, target, poten should, continue and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- the initiation, timing, progress and results of future preclinical studies and clinical trials, and our research and development programs;
- our plans to develop and commercialize our product candidates;
- our collaboration with Celgene Corporation;
- our ability to establish and maintain additional collaborations or obtain additional funding;
- the timing or likelihood of regulatory filings and approvals;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the rate and degree of market acceptance and clinical utility of our products;
- our competitive position;
- our intellectual property position;

developments and projections relating to our competitors and our industry;

the potential of IDH1/IDH2 and pyruvate kinase-R mutations as therapeutic targets;

the potential benefits of our drug candidates targeting IDH1/IDH2 or pyruvate kinase-R mutations, including AG-221, AG-120 and AG-348;

our expectations related to the use of proceeds from this offering; and

our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

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. We have included important factors in the cautionary statements included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, particularly in the Risk factors section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

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You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, and the documents that we have filed as exhibits to the registration statement of which this prospectus supplement is a part completely and with the understanding that our actual future results may be materially different from what we expect. 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.

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Use of proceeds

We estimate that the net proceeds from our issuance and sale of 1,986,455 shares of our common stock in this offering will be approximately $206.7 million after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds will be approximately $237.9 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering as follows:

- approximately $70-100 million to fund the costs of phase 1 clinical development of AG-120, and initiating a global registration program;
- approximately $20-30 million to fund the phase 1/2 clinical development activities for AG-348;
- approximately $50-70 million to fund research and development to advance our pipeline of earlier-stage cancer metabolism and rare genetic disorders programs; and
- the remainder for working capital and other general corporate purposes.

This expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, as well as any additional collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

We believe opportunities may exist from time to time to expand our current business through acquisitions or in-licenses of complementary companies, medicines or technologies. While we have no current agreements, commitments or understandings for any specific acquisitions or in-licenses at this time, we may use a portion of the net proceeds for these purposes.

Pending use of the proceeds as described above, we intend to invest the proceeds in a variety of capital preservation investments, including short-term, interest-bearing, investment-grade instruments and U.S. government securities.

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Price range of common stock

Our common stock began trading on The NASDAQ Global Select Market under the symbol AGIO on July 24, 2013. Prior to that time, there was no public market for our common stock. The following table sets forth the high and low sale prices per share of our common stock, as reported on The NASDAQ Global Select Market, for the periods indicated.

	High	Low
Year Ended December 31, 2013		
Third quarter (from July 24, 2013)	$ 33.45	$ 22.34
Fourth quarter	$ 33.59	$ 15.77
Year Ending December 31, 2014		
First quarter	$ 49.79	$ 21.70
Second quarter	$ 50.37	$ 31.42
Third quarter	$ 69.50	$ 33.01
Fourth quarter (through December 10, 2014)	$ 113.82	$ 58.55

On December 10, 2014, the last reported sale price of our common stock as reported on The NASDAQ Global Select Market was $111.55 per share. As of the date of this prospectus supplement, we had approximately 41 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend policy

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends to holders of common stock in the foreseeable future.

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Capitalization

The following table sets forth our consolidated cash, cash equivalents and marketable securities and capitalization as of September 30, 2014, as follows:

- on an actual basis; and
- on an as adjusted basis to give effect to our issuance and sale of 1,986,455 shares of our common stock in this offering at the public offering price of $110.75 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the following table together with Description of capital stock appearing in the accompanying prospectus, and our consolidated financial statements and related notes to those statements and the Management s Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the year ended December 31, 2013, which is incorporated by reference in this prospectus supplement.

	As of September 30, 2014	
(in thousands, except share and per share data)	**Actual**	**As Adjusted**
Cash, cash equivalents and marketable securities	$ 237,887	$ 444,637
Preferred stock, par value $0.001 per share; 25,000,000 shares authorized, no shares issued or outstanding, actual and as adjusted	$	$
Common stock, par value $0.001 per share; 125,000,000 shares authorized, actual and as adjusted, 34,642,539 shares issued and outstanding, actual; 36,628,994 shares issued and outstanding, as adjusted	$ 35	$ 37
Additional paid-in capital	$ 347,947	$ 554,695
Accumulated other comprehensive income	$ 51	$ 51
Accumulated deficit	$ (140,284)	$ (140,284)
Total stockholders equity	$ 207,749	$ 414,499
Total capitalization	$ 207,749	$ 414,499

The table above does not include:

- 3,816,834 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2014, at a weighted-average exercise price of $13.74 per share;

799,270 shares of common stock reserved as of September 30, 2014, for future issuance under our stock incentive plans; and

327,272 shares of common stock reserved as of September 30, 2014 for future issuance under our 2013 employee stock purchase plan.

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Dilution

As of September 30, 2014, our net tangible book value was approximately $207.7 million, or approximately $6.00 per share. Net tangible book value per share represents the amount of our total tangible assets less total liabilities divided by the 34,642,539 shares of our common stock outstanding as of September 30, 2014. After giving effect to our sale of the shares of common stock in this offering, after deducting underwriting discounts and commissions and estimated offering expenses, the net tangible book value as of September 30, 2014 would have been approximately $414.5 million, or approximately $11.32 per share. This represents an immediate increase in net tangible book value of $5.32 per share to existing stockholders and an immediate dilution in net tangible book value of $99.43 per share to new investors purchasing shares of common stock at the public offering price.

The following table illustrates this dilution on a per share basis:

Public offering price per share		$ 110.75
Net tangible book value per share as of September 30, 2014	$ 6.00	
Increase in net tangible book value per share attributable to new investors	$ 5.32	
Net tangible book value per share as of September 30, 2014 after giving effect to this offering		$ 11.32
Dilution in net tangible book value per share to new investors		$ 99.43

As of September 30, 2014, there were:

3,816,834 shares of common stock issuable upon exercise of stock options outstanding at a weighted-average exercise price of $13.74 per share;

799,270 shares of common stock reserved for future issuance under our stock incentive plans; and

327,272 shares of common stock reserved for future issuance under our 2013 employee stock purchase plan.

To the extent that any of these shares are issued upon exercise of stock options or vesting of restricted stock units, there may be further dilution to new public investors. In addition, the foregoing discussion and table do not take into account further dilution to new investors that could occur upon the issuance of notes in the concurrent notes offering.

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Material U.S. tax considerations for non-U.S. holders of common stock

The following is a general discussion of material U.S. federal income and estate tax considerations relating to the ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term non-U.S. holder means a beneficial owner (other than a partnership or other pass-through entity) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or any state thereof or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus supplement. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus supplement.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder s individual circumstances nor does it address the alternative minimum tax, the Medicare tax on net investment income, or any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt organizations;
- financial institutions;

brokers or dealers in securities;

regulated investment companies;

pension plans;

controlled foreign corporations;

passive foreign investment companies;

owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and

certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or persons who hold their common stock through partnerships or other entities that are pass-through entities for U.S. federal income tax purposes. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

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Dividends

If we pay distributions on our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder s investment, up to such holder s tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading Gain on disposition of common stock. Any such distribution will also be subject to the discussion below under the heading Withholding and information reporting requirements FATCA.

Dividends paid to a non-U.S. holder generally will be subject to U.S. federal withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder s country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder s country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on disposition of common stock

Subject to the discussion below under the heading Withholding and information reporting requirements FATCA, a non-U.S. holder generally will not be subject to U.S. federal income tax on gain recognized on a disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder s conduct of a trade or business in the United States, and if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder will be taxed on a net income basis at the regular graduated rates and in the manner applicable to U.S. persons (as defined in the Code), and if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may also apply;

the non-U.S. holder is a non-resident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition, which may be offset by U.S.-source capital losses of the non-U.S. holder, if any; or

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we are or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder s holding period, if shorter) a U.S. real property holding corporation unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a U.S. real property holding corporation if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a U.S. real property holding corporation for U.S. federal income tax purposes. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rule described above.

Information reporting and backup withholding

The gross amount of the distributions on our common stock paid to each non-U.S. holder and the tax withheld, if any, with respect to such distributions must be reported annually to the IRS. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate, currently 28%, with respect to dividends on our common stock. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable Form W-8) or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under the heading Dividends, will generally be exempt from backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a non-U.S. broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder s U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

Withholding and information reporting requirements FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax of 30% on payments of dividends on, and gross proceeds from the sale or disposition of, our common stock if paid to a foreign entity unless (i) in the case of a foreign entity that is a foreign financial institution (as defined under FATCA), the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) in the case of a foreign entity that is not a foreign financial institution, the foreign entity identifies certain of its U.S. investors, or (iii) the foreign entity is otherwise exempt under FATCA. Under applicable U.S. Treasury Regulations, withholding

under FATCA will generally apply (1) to payments of dividends on our common stock made and (2) to payments of gross proceeds from a sale or other disposition of

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our common stock occurring after December 31, 2016. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of such taxes.

Prospective investors should consult their own tax advisors regarding the possible impact of FATCA on their investment in our common stock and on the entities through which they hold our common stock including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

Federal estate tax

Common stock owned or treated as owned by an individual who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death will generally be included in the individual s gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

The preceding discussion of material U.S. federal tax considerations is for general information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of owning and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

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Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC and Goldman, Sachs & Co. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of Shares
J.P. Morgan Securities LLC	805,492
Goldman, Sachs & Co.	724,943
Cowen and Company, LLC	228,010
Leerink Partners LLC	228,010
Total	1,986,455

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $3.65 per share. After the public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters. The offering of the shares by the underwriters is subject to receipt and acceptance and is subject to the underwriters right to reject any order in whole or in part.

The underwriters have an option to buy up to 297,968 additional shares of common stock. The underwriters have 30 days from the date of this prospectus to exercise this option. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $6.37 per share. The following table shows the per share and total public offering price, underwriting discounts and commissions to be paid to the underwriters and proceeds before expenses to us assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	Per Share	No Exercise	Full Exercise

Public offering price	$ 110.75	$ 219,999,891	$ 252,999,847
Underwriting discounts and commissions to be paid by us	$ 6.37	$ 12,649,994	$ 14,547,491
Proceeds, before expenses, to us	$ 104.38	$ 207,349,897	$ 238,452,356

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $600,000. We have agreed to reimburse the underwriters $30,000 for expenses related to any filing with, and the clearance of this offering by, the Financial Industry Regulatory Authority, Inc.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to

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allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of our common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of our common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC and Goldman, Sachs & Co. for a period of 90 days after the date of this prospectus supplement, other than (A) the shares of our common stock to be sold hereunder, (B) any shares of our common stock issued upon the exercise of options granted under company stock plans or warrants described as outstanding in this prospectus, (C) any options and other awards granted under company stock plans, (D) our filing of a registration statement on Form S-8 or a successor form thereto relating to the shares of our common stock granted pursuant to or reserved for issuance under company stock plans and (E) shares of our common stock or other securities issued in connection with a transaction that includes a commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or not less than a majority or controlling portion of the equity of another entity; provided that the aggregate number of shares of our common stock issued pursuant to clause (E) shall not exceed 5.0% of the total number of outstanding shares of our common stock immediately following the issuance and sale of the underwritten shares pursuant to the underwriting agreement; provided, further, the recipient of any such shares of our common stock and securities issued pursuant to clause (E) during the 90-day restricted period described above shall enter into an agreement substantially in the form described thereby.

Our directors and executive officers have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, for a period of 90 days after the date of this prospectus supplement, may not, without the prior written consent of J.P. Morgan Securities LLC and Goldman, Sachs & Co., (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors and officers in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale, pledge or disposition, (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of our common stock or such other securities, in cash or otherwise or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock, in each case subject to certain exceptions, including (A) transfers of shares of our common stock or other securities as bona fide gifts, (B) transfers or dispositions of shares of our common stock or other securities to any trust for the direct or indirect benefit of the director or officer or the immediate family of such person in a transaction not involving a disposition for value, (C) transfers or dispositions of shares of our common stock or other securities to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which are held by the director or officer or the immediate family of such person in a transaction not involving a disposition for

value, (D) transfers or dispositions of shares of our common stock or other securities by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the director or

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officer, (E) distributions of shares of our common stock or other securities to partners, members or stockholders of the shareholder and (F) the exercise of options to purchase shares of common stock granted under any stock incentive plan described in this prospectus, provided that the underlying common stock issued upon such exercise continues to be subject to the restrictions described herein. In the case of any transfer, disposition or distribution pursuant to clause (A), (B), (C), (D) or (E), each transferee, donee or distributee must execute and deliver to J.P. Morgan Securities LLC and Goldman, Sachs & Co. a lock-up agreement. In addition, in the case of any transfer, disposition or distribution pursuant to clause (A), (B), (C), (D) or (E), no filing by any party under the Exchange Act, or other public announcement may be required or voluntarily made in connection with such transfer, disposition or distribution, other than a filing on a Form 5 made after the expiration of the 90-day restricted period referred to above. In addition, notwithstanding the foregoing restrictions, the director or officer may (i) transfer such person s shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock to us pursuant to any contractual arrangement in effect on the date of the lock-up agreement that provides for the repurchase of such person s common stock or such other securities by us or in connection with such person s termination of employment with us, provided that no filing by any party under the Exchange Act, or other public announcement may be required or voluntarily made in connection with such transfer, other than a filing on a Form 5 made after the expiration of the 90-day restricted period referred to above, (ii) establish a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of common stock, provided that such plan does not provide for any transfers of common stock, except as expressly specified in subsection (iv)(2) below, and provided, further, that except as expressly specified in subsection (iv)(2) below, no filing with the SEC or other public announcement shall be required or voluntarily made by the director or officer or any other person in connection therewith, in each case during the 90-day restricted period or any extension thereof pursuant to the lock-up agreement, and (iii) transfer or dispose of shares of our common stock on the open market following this offering, provided that no filing by any party under the Exchange Act, or other public announcement reporting a reduction in the beneficial ownership of common stock held by the director or officer may be required or voluntarily made in connection with such transfer, other than a filing on a Form 5 made after the expiration of the 90-day restricted period referred to above and (iv) transfer shares of common stock pursuant to sales in the public market undertaken by such person under a trading plan pursuant to Rule 10b5-1 under the Exchange Act, provided that (1) such trading plan shall have been in effect prior to the date of the lock-up agreement, or (2) no shares are transferred pursuant to such trading plan prior to the 60th day after the date of this prospectus supplement and the aggregate number of shares transferred in the aggregate by the undersigned pursuant to this clause (iv)(2) and all other shareholders pursuant to the corresponding exception in their letter agreement with the underwriters relating to the offering does not exceed 50,000 shares during the period commencing on the date ending 60 days after the date of this prospectus supplement and ending at the expiration of the 90-day restricted period and, that to the extent a public announcement or filing under the Exchange Act, if any, is required or voluntarily made by or on behalf of such person or us regarding any such sales, such announcement or filing shall include a statement to the effect that the sale was made pursuant to a trading plan pursuant to Rule 10b5-1 under the Exchange Act.

Holders of a majority of our outstanding common stock have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, for a period ending the earlier of (x) 60 days after the date of this prospectus supplement and (y) February 28, 2015, may not, without the prior written consent of J.P. Morgan Securities LLC and Goldman, Sachs & Co., (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such shareholders in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale, pledge or disposition, (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be

settled by delivery of our common stock or such other securities, in cash or otherwise or (3) make any demand for or exercise any right with respect to the registration

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of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock, in each case subject to certain exceptions, including (A) transfers of shares of our common stock or other securities as bona fide gifts, (B) transfers or dispositions of shares of our common stock or other securities to any trust for the direct or indirect benefit of the shareholder or the immediate family of such person in a transaction not involving a disposition for value, (C) transfers or dispositions of shares of our common stock or other securities to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which are held by the shareholder or the immediate family of such person in a transaction not involving a disposition for value, (D) transfers or dispositions of shares of our common stock or other securities by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the shareholder, and (E) distributions of shares of our common stock or other securities to partners, members or stockholders of the shareholder. In the case of any transfer, disposition or distribution pursuant to clause (A), (B), (C), (D) or (E), each transferee, donee or distributee must execute and deliver to J.P. Morgan Securities LLC and Goldman, Sachs & Co. a lock-up agreement. In addition, in the case of any transfer, disposition or distribution pursuant to clause (A), (B), (C), (D) or (E), no filing by any party under the Exchange Act, or other public announcement may be required or voluntarily made in connection with such transfer, disposition or distribution, other than a filing on a Form 5 made after the expiration of the restricted period referred to above. In addition, notwithstanding the foregoing restrictions, the shareholder may (i) transfer such person s shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock to us pursuant to any contractual arrangement in effect on the date of the lock-up agreement that provides for the repurchase of such person s common stock or such other securities by us or in connection with such person s termination of employment with us, provided that no filing by any party under the Exchange Act, or other public announcement may be required or voluntarily made in connection with such transfer, other than a filing on a Form 5 made after the expiration of the restricted period referred to above, (ii) establish a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of common stock, provided that such plan does not provide for any transfers of common stock, and no filing with the SEC or other public announcement shall be required or voluntarily made by the shareholder or any other person in connection therewith, in each case during the restricted period or any extension thereof pursuant to the lock-up agreement, and (iii) transfer or dispose of shares of our common stock on the open market following this offering, provided that no filing by any party under the Exchange Act, or other public announcement reporting a reduction in the beneficial ownership of common stock held by the shareholder may be required or voluntarily made in connection with such transfer, other than a filing on a Form 5 made after the expiration of the restricted period referred to above.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

Our common stock is listed on The NASDAQ Global Select Market under the symbol AGIO.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters option referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in

the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

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The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The NASDAQ Global Select Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on The NASDAQ Global Select Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The NASDAQ Global Select Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker s average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

The underwriters and their respective affiliates are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to our assets, securities and/or instruments (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Selling restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus

supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

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United Kingdom

Each underwriter has represented and agreed that:

(1) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of our common shares in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(2) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to our common shares in, from or otherwise involving the United Kingdom.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), an offer to the public of any shares which are the subject of the offering contemplated by this prospectus (the Shares) may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any Shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(1) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(2) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

(3) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of Shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to the public in relation to any Shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase any Shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to professional investors within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement,

invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

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Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

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Legal matters

The validity of the shares of common stock offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Davis Polk & Wardwell LLP, New York, New York, has acted as counsel for the underwriters in connection with certain matters relating to this offering.

Experts

The consolidated financial statements of Agios Pharmaceuticals, Inc. appearing in Agios Pharmaceuticals, Inc. s Annual Report on Form 10-K for the year ended December 31, 2013 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report included therein, and incorporated herein by reference. Such consolidated financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

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Where you can find more information

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC s website at http://www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.agios.com. Our website is not a part of this prospectus supplement and is not incorporated by reference in this prospectus. You may also read and copy any document we file at the SEC s Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement and the accompanying prospectus omit some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus supplement and in the accompanying prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

Incorporation of documents by reference

The SEC allows us to incorporate by reference into this prospectus supplement much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement and the accompanying prospectus are continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement and the accompanying prospectus incorporate by reference the documents listed below (File No. 001-36014) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2013, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2014 Annual Meeting of Stockholders;

- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2014, June 30, 2014 and September 30, 2014;

- Current Reports on Form 8-K filed April 7, 2014, April 17, 2014, May 14, 2014, June 3, 2014, June 13, 2014, June 16, 2014, September 19, 2014, October 15, 2014 (solely with respect to the 58th slide, titled IDH Mutations Also Found in MDS, NHL and Range of Solid Tumors in Exhibit 99.1), November 19, 2014, November 26, 2014, December 8, 2014, December 8, 2014 and December 10, 2014; and

The description of our common stock contained in our Registration Statement on Form 8-A filed on July 19, 2013, including any amendments or reports filed for the purpose of updating such description.

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You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Investor Relations

Agios Pharmaceuticals, Inc.

38 Sidney Street, 2nd Floor

Cambridge, MA 02139

(617) 649-8600

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PROSPECTUS

Debt Securities

Common Stock

Preferred Stock

Warrants

We may offer and sell securities from time to time in one or more offerings. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference herein or therein carefully before you invest. This prospectus may not be used to offer and sell our securities unless accompanied by a prospectus supplement.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on The NASDAQ Global Select Market under the symbol AGIO .

Investing in these securities involves certain risks. See Risk Factors included in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is December 9, 2014

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We have not authorized anyone to provide any information or to make any representations other than those contained or incorporated by reference in this prospectus, any prospectus supple