AGIOS PHARMACEUTICALS INC
Form 424B5
September 13, 2016
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The information in this preliminary prospectus supplement is not complete and may be changed. The registration statement filed with the Securities and Exchange Commission relating to these securities is effective. This preliminary prospectus supplement is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state or jurisdiction where the offer or sale is not permitted.

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

Subject to completion, dated September 13, 2016

Preliminary prospectus supplement

(To Prospectus dated December 9, 2014)

$150,000,000

Common Stock

Agios Pharmaceuticals, Inc. is offering 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 September 12, 2016 was $45.80 per share.

Investing in our common stock involves risks. See Risk factors beginning on page S-15 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	$	$
Underwriting discounts(1)	$	$
Proceeds, before expenses, to Agios Pharmaceuticals, Inc.	$	$

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. See Underwriting beginning on page S-26 of this prospectus supplement.

We have granted the underwriters the right to purchase up to an additional $22,500,000 of 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.

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 September , 2016.

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

The date of this prospectus supplement is September , 2016.

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PROSPECTUS SUPPLEMENT

PROSPECTUS

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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 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-15 and the risk factors contained in our Annual Report on Form 10-K for the year ended December 31, 2015 and our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2016.

Overview

We are a biopharmaceutical company committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and rare genetic metabolic disorders, or RGDs, which are a subset of orphan genetic metabolic diseases. Metabolism is a complex biological process involving the uptake and assimilation of nutrients in cells to produce energy and facilitate many of the processes required for cellular division and growth. We focus our efforts on using cellular metabolism, an unexploited area of biological research with disruptive potential, as a platform for developing potentially transformative small molecule medicines. Our most advanced cancer product candidates are AG-221 and AG-120, which target mutated isocitrate dehydrogenase 2 and 1, or IDH2 and IDH1, respectively, and AG-881, which targets both mutated IDH1 and mutated IDH2. These mutations are found in a wide range of hematological malignancies and solid tumors. On September 7, 2016, our collaboration partner Celgene Corporation, or Celgene, announced that it expects to submit a new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for enasidenib (AG-221) in relapsed and/or refractory acute myeloid leukemia, or AML, by year-end 2016. The NDA will be based on data from the ongoing phase 1/2 study of AG-221 in patients with advanced hematologic malignancies with an IDH2 mutation. We plan to explore a similar regulatory path for AG-120 which could lead to an NDA submission in the U.S. in 2017, and plan to provide a regulatory update on AG-120 by the end of 2016. Our lead product candidates in our RGD programs, AG-348 and AG-519, target pyruvate kinase-R for the treatment of pyruvate kinase, or PK, deficiency. PK deficiency is a rare disorder that often results in severe hemolytic anemia due to inherited mutations in the pyruvate kinase enzyme within red blood cells. In June 2016, at the 21st Congress of the European Hematology Association, or EHA, we presented initial data showing that AG-348 had achieved proof-of-concept in DRIVE-PK, our ongoing phase 2 study of AG-348. Also at EHA in June, we presented initial data from our ongoing phase 1 study of AG-519 in healthy volunteers, showing that AG-519 had demonstrated early proof-of-mechanism. We expect to select either AG-348 or AG-519 for pivotal development by the end of 2016.

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. 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.

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 clinical data of

AG-221 and AG-120, our lead inhibitors of mutant IDH2 and

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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.

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 September 7, 2016, Celgene announced that it expects to submit a NDA to the FDA for enasidenib (AG-221) in relapsed and/or refractory AML by year-end 2016. The NDA will be based on data from the ongoing phase 1/2 study of AG-221 in patients with advanced hematologic malignancies with an IDH2 mutation.

In December 2015, we reported clinical data, as of September 1, 2015, from the dose escalation phase and expansion cohorts of the ongoing phase 1 clinical trial, which was transitioned to a phase 1/2 trial in May 2015, evaluating single agent AG-221, which included 209 response-evaluable enrolled patients with IDH2 mutant-positive AML. The new data were presented at the 2015 American Society of Hematology (ASH) Annual Meeting and Exposition in Orlando, Florida and showed investigator-assessed objective responses in 79 out of 209 response-evaluable patients. Of the 79 patients who achieved an objective response, there were 37 complete remissions (CR), three complete remissions with incomplete platelet recovery (CRp), 14 marrow complete remissions (mCR), three complete remissions with incomplete hematologic recovery (CRi) and 22 partial remissions (PR). A CR is determined by using well-established criteria, which requires no evidence of leukemia in the bone marrow and blood accompanied by full restoration of all blood counts to normal ranges. A CRp means all the criteria for CR are met except that platelet counts are outside of the normal range. Platelets are one of the three major types of blood cells. A mCR means that there is no evidence for leukemia in the marrow but the blood counts have not fully restored. A CRi means there is no evidence for leukemia in the marrow but the neutrophils, a subset of white blood cells responsible for fighting bacterial infections, are outside the normal range. A PR means all the criteria for CR are met except that the immature defective blood cells, or leukemia, in the bone marrow are in the 5% to 25% range and have been decreased by at least 50% over pretreatment. Of the 159 patients with relapsed or refractory AML, 59 achieved an objective response, including 29 CRs, one CRp, nine mCRs, three CRis and 17 PRs. Of the 24 patients with AML who declined standard of care chemotherapy, 10 achieved an objective response, including four CRs, one CRp, one mCR and four PRs. Of the 14 patients with myelodysplastic syndromes, or MDS, seven achieved an objective response, including three CRs, one CRp and three mCRs. Responding relapsed or refractory AML patients were on the trial for up to 18 months with a median duration of treatment of 6.8 months, ranging from 1.8 to 18 months. Responses were durable, with median response duration of 6.9 months in patients with relapsed or refractory AML. A safety analysis was conducted for all 231 treated patients. The majority of AEs reported by investigators were mild to moderate, with the most common being nausea, diarrhea, fatigue and febrile neutropenia. The serious adverse events, or SAEs, observed during the trial were mainly disease related. Twenty-three percent of patients had treatment-related SAEs, including notably differentiation syndrome (4 percent), leukocytosis (4 percent) and nausea (2 percent). Drug-related Grade 5 SAEs included atrial flutter (one patient), cardiac tamponade (one patient), pericardial effusion (one patient) and respiratory failure (one patient). Dose escalation has been completed and a maximum tolerated dose, or MTD, has not been reached. The ongoing AG-221 phase 1/2 trial includes a dose-escalation phase and the following five expansion cohorts, all of which have completed accrual: (i) a cohort of 25 patients aged 60 years or older with IDH2 mutant-positive relapsed or refractory AML, or any IDH2-mutant positive AML patient, regardless of age, who has relapsed following a bone marrow transplant (BMT); (ii) a cohort of 25 patients aged less than 60 years with IDH2 mutant-positive relapsed or refractory AML, not including patients with AML who have relapsed following a BMT; (iii) a cohort of 25 patients aged 60 years or older with untreated IDH2 mutant-positive AML who decline standard of care chemotherapy; (iv) a cohort of 25 patients with IDH2 mutant-positive advanced hematologic malignancies not eligible for cohorts (i) to (iii); and (v) a

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cohort of approximately 125 patients with IDH2 mutant-positive AML who are in second or later relapse, refractory to second-line induction or reinduction treatment, or have relapsed after allogeneic transplantation. AG-221 continued to show favorable drug exposure and pharmacokinetics at all doses tested with substantial reductions in plasma levels of 2HG, which is produced by the mutated IDH2 and IDH1 proteins, to the level observed in healthy volunteers. In the second half of 2016, Celgene , in collaboration with us, intends to initiate an expansion arm of our phase 1/2 clinical trial, evaluating AG-221 in high-risk MDS patients.

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

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

In June 2014, the FDA granted us orphan drug designation for AG-221 for treatment of patients with AML, and in August 2014, we announced that the FDA granted fast track designation to AG-221 for treatment of patients with AML that harbor an IDH2 mutation. In April 2016, we and Celgene received European Medicines Agency, or EMA, Orphan Drug Designation for AG-221 for the treatment of AML.

Celgene maintains worldwide development and commercial rights to AG-221 and Celgene will fund the future development and commercialization costs related to this program.

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 hematologic and solid tumor cancers, including AML, chondrosarcoma and cholangiocarcinoma where both the treatment options and prognosis for patients are poor. In May 2016, Celgene transferred its rights to AG-120 outside of the United States to us and we are now responsible for global development of the compound. On September 7, 2016, in connection with Celgene s announcement of plans to submit a NDA for AG-221 in relapsed and/or refractory AML by the end of 2016, we announced that we plan to explore a similar regulatory path for AG-120, which could lead to an NDA submission for AG-120 in the U.S. in 2017. We plan to provide a regulatory update on AG-120 by the end of 2016.

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

for AG-120 for treatment of patients with AML.

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

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

In December 2015, we reported data, as of October 1, 2015, from the ongoing phase 1 clinical trial evaluating single agent AG-120, which included 87 enrolled patients with IDH1 mutant-positive advanced hematologic malignancies, of which 78 were from the dose-escalation phase and nine were from the expansion phase. The data were presented at the 2015 ASH Annual Meeting and Exposition in Orlando, Florida and showed investigator-assessed objective responses in 27 out of 78 response-evaluable patients on AG-120. Of the 27 patients who achieved an objective response, there were 12 CRs, seven CRps, six mCRs, one CRi and one PR. Patients were on the trial treatment for up to 14.1 months, with a median duration of treatment of 2.9 months, ranging from 0.1 to 14.1 months. Data continued to show durable clinical activity for AG-120, with responses maintained for up to 12.5 months and a median duration of response of 5.6 months. AG-120 continued to show favorable drug exposure and pharmacokinetics at all doses tested and also substantially reduced plasma levels of 2HG to the level observed in healthy volunteers. The mechanism of response is consistent with differentiation, as evidenced by the maturation of the leukemic cells into infection fighting white blood cells, or neutrophils. The majority of AEs reported by investigators were mild to moderate, with the most common being fatigue, diarrhea, pyrexia and nausea. A MTD has not been reached, and dose escalation is now complete. As described above, in December 2015, we announced the initiation of a phase 1b, multicenter, international, open-label clinical trial of AG-221 or AG-120 in combination with induction and consolidation therapy in patients with newly diagnosed AML with an IDH mutation who are eligible for intensive chemotherapy.

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

We intend to initiate a global registration-enabling phase 3 clinical trial in frontline AML patients who harbor an IDH1 mutation in the first half of 2017. In addition, we intend to initiate a randomized phase 2 clinical trial of AG-120 in patients with IDH1 mutant-positive cholangiocarcinoma in the second half of 2016.

We have worldwide development and commercial rights to AG-120 and expect to fund future development and commercialization costs related to this program.

AG-881: pan-IDH program

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

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

Rare Genetic Disease Portfolio- Pyruvate Kinase Deficiency

PK deficiency, a rare genetic disorder, manifests as mild to severe forms of anemia caused by excessive premature destruction of red blood cells. PKR is the isoform of pyruvate kinase that is present in 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). The current standard of care for PK deficiency is supportive, including blood transfusions, splenectomy, chelation therapy to address iron overload and/or interventions for other treatment- and disease-related morbidities. There is no approved therapy to treat the underlying cause of PK deficiency.

PK deficiency is an autosomal recessive disease whereby all patients inherit two mutations, one from each parent. More than 250 different mutations have been identified to date. The mutations observed in PK deficiency patients are classified in two main categories. A missense mutation causes a single amino acid change in the protein, generally resulting in some functional protein. A non-missense mutation is any mutation other than a missense mutation, generally resulting in little functional protein. It is estimated that 53 percent of patients with PK deficiency have two

missense mutations, 25 percent have one missense and one non-missense mutation, and 22 percent have two non-missense mutations.

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Boston Children s Hospital, in collaboration with us, is conducting a Natural History Study to better understand the symptoms and complications of PK deficiency, identify patients and treatment centers, and capture other clinical data, including quality of life measures and genetic information. We believe our lead product candidates have the potential to address up to a minimum of approximately 80% of patients who harbor at least one missense mutation. In addition, some of our compounds have demonstrated efficacy in patients with non-missense mutations preclinically, albeit to a lesser extent. We expect to select either AG-348 or AG-519 for pivotal development by the end of 2016.

AG-348: lead pyruvate kinase (PK) deficiency program

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

In June 2015, we initiated DRIVE PK, a global phase 2, first-in-patient, open-label safety and efficacy clinical trial of AG-348 in adult, transfusion-independent patients with PK deficiency. The multi-center, randomized trial includes two arms with 25 patients each. The patients in the first arm receive 50 mg twice daily, and the patients in the second arm receive 300 mg twice daily. The trial includes a six-month dosing period with the opportunity for continued treatment beyond six months based on safety and clinical activity.

In June 2016, we reported the first clinical data from DRIVE PK at EHA in Copenhagen, Denmark. These data established proof of concept for AG-348 as a novel, first-in-class, oral activator of both wild-type and mutated PKR enzymes. Results presented were as of the March 27, 2016 data cut-off and were from 18 transfusion independent patients treated with twice-daily dosing for up to six months. The data showed that AG-348 was well tolerated, and no patients discontinued treatment early. The majority of adverse events, or AEs, were mild to moderate and transient. One patient received a dose reduction due to rapidly increasing hemoglobin. This patient was dose-reduced from 300 mg to 50 mg and remained on study. One Grade 2 AE of osteoporosis was reported after the cut-off date. This patient had osteopenia at baseline assessment. Sex steroids were assessed at baseline, week 12 and week 24. Free testosterone and estradiol were available for four and five male patients, respectively. An upward trend in free testosterone and a downward trend in estradiol were observed in these patients. Due to the small number of female patients with hormone data, only data from male patients were reported. Additional data and longer follow up are needed to determine if hormonal changes are clinically significant. In the study, nine of 18 patients, including nine of 13 patients with at least one missense mutation, demonstrated robust, rapid and sustained increases in hemoglobin as evidenced by an increase in hemoglobin of greater than 1.0 g/dL. Both doses of AG-348 demonstrated clinical activity, with four patients in the 50 mg group and five patients in the 300 mg group experiencing increases of greater than 1.0 g/dL. In patients who had hemoglobin increases of greater than 1.0 g/dL, the mean maximum hemoglobin increase was 3.4 g/dL (range 2.3 4.9 g/dL). The median time to a hemoglobin increase of greater than 1.0 g/dL was 1.9 weeks (range 1.1 9.1 weeks). None of the five patients with two non-missense mutations showed increases in hemoglobin of greater than 1.0 g/dL. Further data are needed to obtain a greater understanding of the relationship between genotype and response. Additionally, pharmacokinetics was favorable and consistent with those observed in healthy volunteers. Pharmacodynamics data did not demonstrate a correlation with hemoglobin increases and ATP elevation. More data are needed to clarify if any correlation exists between 2,3-DPG decreases and Hb increases of greater than 1.0 g/dL. Enrollment for this trial is ongoing.

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

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AG-519: a second novel PKR activator

AG-519 is an orally available small molecule and our second product candidate that is a potent activator of the PKR enzyme, with comparable biochemical, cellular and in-vivo activity to AG-348. We initiated a placebo-controlled phase 1 clinical trial of AG-519 in healthy volunteers in the first quarter of 2016. This trial is an integrated single ascending dose, or SAD, and multiple ascending dose, or MAD, trial.

In June 2016, we reported the first clinical data from this trial at EHA in Copenhagen. These results provided proof-of-mechanism for AG-519, a potent, oral, selective PKR activator. In the SAD portion of the trial, four cohorts with doses of AG-519 ranging from 50 mg to 1250 mg were tested against placebo in 32 healthy volunteers and demonstrated a favorable safety profile in all doses tested. There were no SAEs reported, and all AEs were mild to moderate, with the most common being headache. In addition, there were no early discontinuations due to AG-519 and the maximum tolerated dose was not reached. Mean decreases in blood 2,3-DPG levels, up to 43 percent from baseline were observed in the SAD cohorts, reaching minimum levels after 24 hours. As expected, ATP levels did not change after a single dose of AG-519, consistent with phase 1 SAD findings from AG-348. Healthy volunteers receiving placebo showed no changes in 2,3-DPG or ATP levels. In the MAD portion of the trial, the first two cohorts reported data from 16 healthy volunteers dosed twice daily with 125 mg or 375 mg of AG-519 or placebo for 14 days. There were no SAEs reported, with all AEs being mild to moderate, and the most common being headache. One subject receiving AG-519 at the 375 mg dose experienced a low blood platelet count (Grade 2 thrombocytopenia) on Day 14. Platelet levels started to recover within five days of the last dose and returned to normal levels seven days after the last dose. Since the EHA data presentation, 18 additional healthy volunteers have been dosed with AG-519 for 14 days, and there have been no additional reported cases of low blood platelet count (thrombocytopenia). Pharmacodynamic data from these MAD cohorts showed a mean decrease of up to 47 percent in blood 2,3-DPG levels and a mean increase of up to 62 percent in blood ATP levels from baseline. In contrast, healthy volunteers receiving placebo showed no changes in 2,3-DPG or ATP levels. Subjects treated with AG-519 exhibited no significant changes in sex steroids levels, consistent with a lack of aromatase enzyme inhibition. Enrollment into additional MAD cohorts is ongoing.

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

Collaborations with Celgene

In April 2010, we entered into a discovery and development collaboration and license agreement, or the 2010 Agreement, with Celgene, focused on targeting cancer metabolism. The goal of the collaboration under the 2010 Agreement is to discover, develop and commercialize disease-altering therapies in oncology arising out of our cancer metabolism research platform that have achieved development candidate status. The discovery phase of the collaboration under the 2010 Agreement expired in April 2016. Under the terms of the 2010 Agreement, we led research, preclinical and early development efforts through phase 1, while Celgene received an option to obtain exclusive rights either upon Investigational New Drug application, or IND, acceptance or at the end of phase 1 to further develop and commercialize medicines emerging from our cancer metabolism research. Celgene leads and funds global development and commercialization of development candidates for which it exercised its option to obtain a co-commercialization license, and we retained development and commercialization rights in the United States for development candidates for which we exercised our option to retain a split license. On all programs under the 2010 Agreement for which Celgene exercised its option, we are eligible to receive up to $120 million in milestone-based payments as well as royalties on any sales.

We nominated AG-221 and AG-120 during the discovery phase of the collaboration under the 2010 Agreement. In June 2014, Celgene exercised its exclusive option to license worldwide development and commercialization

rights for AG-221. In addition to contributing our scientific and translational expertise, we continued to conduct certain clinical development and regulatory activities within the AG-221 development program while transitioning responsibilities to Celgene, which leads later development activities. In the first quarter of 2015,Celgene exercised its exclusive option to license development and commercialization rights to AG-120 outside the United States. Following Celgene s exercise of this option, we retained development and commercialization rights for AG-120 in the United States. In May 2016, Celgene transferred its rights to AG-120 outside the United States to us and we are now wholly responsible for global development of AG-120.

During April 2015, we selected a third novel IDH mutant inhibitor, AG-881, for clinical development. On April 27, 2015, we entered into a joint worldwide development and profit share collaboration and license agreement with Celgene, and our wholly owned subsidiary, Agios International Sarl, which was organized in Switzerland in April 2015, entered into a collaboration and license agreement with Celgene International II Sarl. We refer to these agreements collectively as the AG-881 agreements. The AG-881 agreements establish a worldwide collaboration focused on the development and commercialization of AG-881 products. Under the terms of the AG-881 agreements, we received initial upfront payments totaling $10 million in May 2015 and are eligible to receive up to $70 million in milestone-based payments. We and Celgene will equally split all worldwide development costs, subject to specified exceptions, as well as any profits from any net sales of, or commercialization losses related to, licensed AG-881 products.

In May 2016, at the same time that we and Celgene amended the 2010 agreement, we entered into a new global research and collaboration agreement with Celgene and Celgene RIVOT Ltd., a wholly owned subsidiary of Celgene, which we refer to as the 2016 agreement, focused on metabolic immuno-oncology, an emerging field of cancer research focused on altering the metabolic state of immune cells to enhance the body s immune response to cancer. The initial four-year research term of the 2016 agreement will expire on May 17, 2020. Celgene may extend the research term for up to two, or in specified cases, up to four, additional one-year terms by paying us a $40 million per-year extension fee. During the research term of the 2016 agreement, we plan to conduct research programs focused on discovering compounds that are active against metabolic targets in the immuno-oncology, or IO, field.

We have granted Celgene the right to obtain exclusive options to development and commercialization rights for each program that Celgene has designated for further development, under the 2016 agreement. Research programs that have applications in the inflammation and autoimmune, or I&I, field that may result from the 2016 agreement will also be subject to the exclusive options described above. We will retain rights to any program that Celgene does not designate for further development or as to which Celgene does not exercise its option.

Under the terms of the 2016 agreement, Celgene made an initial $200 million upfront payment to us for the initial four-year research term. Celgene will pay us an $8 million designation fee for each program that Celgene designates for further development. For each program as to which Celgene exercises its option to develop and commercialize, subject to antitrust clearance, Celgene will pay us an option exercise fee of at least $30 million. In certain cases, Celgene may exercise its option to develop and commercialize two early-stage I&I programs, prior to Celgene designating the program for further development, by paying us an option exercise fee of $10 million.

We and Celgene will split all worldwide development costs, subject to specified exceptions, as well as any profits from any net sales of, or commercialization losses related to, licensed products in the IO field. Celgene has the option to designate one program in the IO field as the 65/35 program, for which Celgene will be the lead party for the United States and will have a 65% profit or loss share. For programs in the IO field other than the 65/35 program, we and Celgene will alternate, on a program-by-program basis, being the lead party for the United States, with Agios having the right to be the lead party for the first such program where each party will have a 50% profit or loss share. We are eligible to receive up to $169 million in milestone payments for each

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50/50 program and up to $209 million for the 65/35 program. Celgene will be responsible for all worldwide development costs, subject to specified exceptions, as well as worldwide commercialization costs, for licensed products in the I&I field. We are eligible to receive royalties at tiered, double-digit percentage rates on Celgene s net sales, if any, of applicable licensed products in the I&I field and up to $386 million in milestone payments for each such program.

In addition to new programs identified under the 2016 agreement, we and Celgene have also agreed that all future development and commercialization of two cancer metabolism programs that were conducted under the 2010 agreement will now be governed by the 2016 agreement. One of these cancer metabolism programs is focused on MTAP deleted cancers. MTAP (methylthioadenosine phosphorylase) is a metabolic enzyme that is deleted in approximately 15 percent of all cancers. This deletion is readily detected by a simple genomic test, thus allowing the selection of patients predicted to be sensitive to the therapy. Agios scientists have discovered a novel pathway comprised of multiple targets with a shared vulnerability in MTAP-deleted tumors and have demonstrated that this pathway can be modulated by small molecule inhibitors, resulting in robust anti-tumor activity in animal models.

Subsequent to the execution of the 2016 agreement, Celgene and we agreed to terminate the 2010 agreement, effective as of August 15, 2016, as to the program directed to the IDH1 target, for which AG-120 is the lead development candidate. Under the 2010 agreement, Celgene had held development and commercialization rights to the IDH1 program outside of the United States, and we held such rights inside the United States. As a result of the termination, we obtained global rights to AG-120 and the IDH1 program. Neither party will have any financial obligation, including royalties or milestone payments, to the other concerning AG-120 or the IDH1 program after final reconciliation of specified shared development costs. Under the terms of the termination, the parties are released from their exclusivity obligations under the 2010 agreement with respect to the IDH1 program. The AG-120 termination does not alter our global collaboration with Celgene pursuant to the AG-881 agreements concerning AG-881, which is directed at both the IDH1 target and the IDH2 target.

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 RGDs. Key elements of our strategy include:

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

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

- Collaborating closely with the FDA and other regulatory bodies to aggressively pursue early registration potential for our product candidates, for example by exploring a similar regulatory path for AG-120 as Celgene is for AG-221.

- Continuing to build a product engine for cancer and RGDs 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.

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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 RGDs. 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.
- 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 June 30, 2016, we had an accumulated deficit of $363.8 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 may not result in compounds that are useful in treating cancer or RGDs, 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 collaborations with Celgene and may depend on collaborations with additional third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

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 own issued patents for two of our lead product candidates, AG-348 and AG-519, in the United States, and do not own or license any issued patents for any of our other lead product candidates. If we do not, or are unable to, obtain or maintain any issued patents for any of our lead product candidates, it could have a material adverse effect on our competitive position, business, financial condition, results of operations, and prospects.

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If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our corporate information

We were incorporated under the laws of the State of Delaware in August 2007. Our executive offices are located at 88 Sidney Street, 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	shares
Common stock to be outstanding after this offering	shares
Option to purchase additional shares	The underwriters have an option for a period of 30 days to purchase up to $22,500,000 of additional shares of our common stock.
Use of proceeds	We intend to use the net proceeds from this offering for working capital and general corporate purposes, including ongoing late stage development and pre-commercial activities for both AG-120 and AG-221, advancement of our PK deficiency program, and development of our early candidate programs. See Use of proceeds for more information.
Risk factors	See Risk factors beginning on page S-15 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 38,029,510 shares of our common stock outstanding as of June 30, 2016.

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

- 5,383,189 shares of common stock issuable upon exercise of stock options outstanding as of June 30, 2016 at a weighted-average exercise price of $45.85 per share;
- 66,300 shares of common stock issuable upon vesting of restricted stock units outstanding as of June 30, 2016;

115,270 shares of common stock issuable upon vesting of performance-based stock units outstanding as of June 30, 2016;

981,516 shares of common stock reserved as of June 30, 2016 for future issuance under our equity incentive plans; and

297,795 shares of common stock reserved as of June 30, 2016 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.

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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 six months ended June 30, 2016 and the consolidated balance sheet data as of June 30, 2016 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 June 30, 2016. We derived the consolidated statement of operations data for the years ended December 31, 2015, 2014 and 2013 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, 2015. 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, 2015 and our unaudited Quarterly Report on Form 10-Q for the six months ended June 30, 2016 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.

	Six months ended June 30, 2016	Year Ended December 31, 2015	2014	2013
(in thousands, except share and per share amounts)				
Consolidated statement of operations data:				
Collaboration Revenue related party	$ 38,259	$ 59,119	$ 65,358	$ 25,548
Operating expenses:				
Research and development	94,842	141,827	100,371	54,502
General and administrative	23,481	35,992	19,120	9,929
Total operating expenses	118,323	177,819	119,491	64,431
Loss from operations	(80,064)	(118,700)	(54,133)	(38,883)
Interest income	913	968	203	55
Loss before provision (benefit) for income taxes	(79,151)	(117,732)	(53,930)	(38,828)
Provision (benefit) for income taxes			(426)	579
Net loss	(79,151)	(117,732)	(53,504)	(39,407)
Cumulative preferred stock dividends				(4,162)
Net loss applicable to common stockholders	$ (79,151)	$ (117,732)	$ (53,504)	$ (43,569)
Net loss per share applicable to common stockholders basic and diluted	$ (2.09)	$ (3.15)	$ (1.59)	$ (2.83)

Weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted	37,910,233	37,429,262	33,667,024	15,415,373

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	As of June 30, 2016	
(in thousands)	**Actual**	**As Adjusted(1)**
Condensed consolidated balance sheet data:		
Cash, cash equivalents and marketable securities	$ 512,295	$
Total assets	557,601	
Total liabilities	268,523	
Common stock	38	
Additional paid-in capital	652,574	
Accumulated deficit	(363,831)	
Total stockholders equity	289,078	

(1) The as adjusted condensed 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 $ 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, 2015 and our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2016, 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 significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that 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 $ per share, after giving effect to the sale by us of shares in this offering at the public offering price of $ 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 regarding:

- the initiation, timing, progress and results of current and future preclinical studies and clinical trials, and our research and development programs;
- the potential of IDH1/IDH2 and pyruvate kinase-R mutations as therapeutic targets;
- the potential benefits of our product candidates targeting IDH1/IDH2 or pyruvate kinase-R mutations, including AG-120, AG-221, AG-881, AG-348 and AG-519;
- our plans to develop and commercialize our product candidates;
- our collaborations 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;

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 $150,000,000 of shares of our common stock in this offering will be approximately $ million after deducting the estimated 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 $ million, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for working capital and general corporate purposes, including ongoing late stage development and pre-commercial activities for both AG-120 and AG-221, advancement of our PK deficiency program, and development of our early candidate programs.

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, U.S. government securities and highly rated corporate debt securities.

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Price range of common stock

Our common stock is listed on The NASDAQ Global Select Market under the symbol AGIO. 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
2014		
First Quarter	$ 49.79	$ 21.70
Second Quarter	$ 50.37	$ 31.42
Third Quarter	$ 69.50	$ 33.01
Fourth Quarter	$ 124.39	$ 58.55
2015		
First quarter	$ 138.85	$ 88.03
Second quarter	$ 126.35	$ 90.58
Third quarter	$ 120.96	$ 67.52
Fourth quarter	$ 81.77	$ 48.00
2016		
First quarter	$ 66.87	$ 33.50
Second quarter	$ 66.74	$ 39.36
Third quarter (through September 12, 2016)	$ 48.00	$ 35.84

On September 12, 2016, the last reported sale price of our common stock as reported on The NASDAQ Global Select Market was $45.80 per share. As of the date of this prospectus supplement, we had approximately 21 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 June 30, 2016, as follows:

- on an actual basis; and
- on an as adjusted basis to give effect to our issuance and sale of shares of our common stock in this offering at the public offering price of $ per share, after deducting estimated 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, 2015, which is incorporated by reference in this prospectus supplement.

	As of June 30, 2016	
(in thousands, except share and per share data)	Actual	As Adjusted
Cash, cash equivalents and marketable securities	$ 512,295	$
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, 38,029,510 shares issued and outstanding, actual; shares issued and outstanding, as adjusted	$ 38	$
Additional paid-in capital	$ 652,574	$
Accumulated other comprehensive income	$ 297	$ 297
Accumulated deficit	$ (363,831)	$ (363,831)
Total stockholders equity	$ 289,078	$
Total capitalization	$ 289,078	$

The table above does not include:

- 5,383,189 shares of common stock issuable upon exercise of stock options outstanding as of June 30, 2016, at a weighted-average exercise price of $45.85 per share;
- 66,300 shares of common stock issuable upon vesting of restricted stock units outstanding as of June 30, 2016;
- 115,270 shares of common stock issuable upon vesting of performance-based stock units outstanding as of June 30, 2016;

981,516 shares of common stock reserved as of June 30, 2016, for future issuance under our stock incentive plans; and

297,795 shares of common stock reserved as of June 30, 2016 for future issuance under our 2013 employee stock purchase plan.

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Dilution

As of June 30, 2016, our net tangible book value was approximately $289.1 million, or approximately $7.60 per share. Net tangible book value per share represents the amount of our total tangible assets less total liabilities divided by the 38,029,510 shares of our common stock outstanding as of June 30, 2016. After giving effect to our sale of the shares of common stock in this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses, the net tangible book value as of June 30, 2016 would have been approximately $ million, or approximately $ per share. This represents an immediate increase in net tangible book value of $ per share to existing stockholders and an immediate dilution in net tangible book value of $ 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		$
Net tangible book value per share as of June 30, 2016	$ 7.60	
Increase in net tangible book value per share attributable to new investors	$	
Net tangible book value per share as of June 30, 2016 after giving effect to this offering		$
Dilution in net tangible book value per share to new investors		$

As of June 30, 2016, there were:

- 5,383,189 shares of common stock issuable upon exercise of stock options outstanding at a weighted-average exercise price of $45.85 per share;
- 66,300 shares of common stock issuable upon vesting of restricted stock units outstanding;
- 115,270 shares of common stock issuable upon vesting of performance-based stock units outstanding;
- 981,516 shares of common stock reserved for future issuance under our stock incentive plans; and
- 297,795 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 or performance-based stock units, there may be further dilution to new public investors.

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

The following is a 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 or differing interpretation 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 other entities that are pass-through entities for U.S. federal income tax purposes or persons who hold their common stock through partnerships or other pass-through entities. 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 acquisition, ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

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Prospective non-U.S. holders of our common stock should consult their own tax advisors regarding the U.S. federal, state, local and non-U.S. income and other tax considerations of acquiring, holding and disposing of our common stock.

Distributions on our common stock

As discussed under Dividend policy above, we do not expect to make cash dividends to holders of our common stock in the foreseeable future. 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 distributions will also be subject to the discussions below under the headings Information reporting and backup withholding and 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 (generally including provision of a valid IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the non-U.S. holder s conduct of a trade or business within the United States). 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 classified as a corporation for U.S. federal income tax purposes 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 and the specific methods available to them to satisfy these requirements.

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

In general (subject to the discussion below under the headings Information reporting and backup withholding and FATCA), a non-U.S. holder will not be subject to U.S. federal income tax or withholding tax on gain realized upon such holder s sale, exchange or other disposition of shares 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

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applicable to U.S. persons (as defined in the Code), and if the non-U.S. holder is a foreign corporation, the branch profits tax described above under the heading Distributions on our common stock also may 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

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 and to each non-U.S. holder. Non-U.S. holders generally will 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 non-U.S. 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 Distributions on our common stock, will generally be exempt from U.S. 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 broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a 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. Rather, 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.

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FATCA

Provisions of the Code commonly known as the Foreign Account Tax Compliance Act, or FATCA, generally impose a U.S. federal withholding tax at a rate of 30% on payments of dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign entity unless: (i) if the foreign entity is a foreign financial institution, the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a foreign financial institution, the foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA.

Withholding under FATCA generally (1) applies to payments of dividends on our common stock and (2) will apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2018. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock and 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.

U.S. federal estate tax

Shares of our common stock that are 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 are considered U.S. *situs* assets and will be included in the individual s gross estate for U.S. federal estate tax purposes. Such shares, 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 information only. It is not legal or 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 purchasing, holding 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	
Goldman, Sachs & Co	
Total	

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 $ 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 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 $ 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	$	$	$
Underwriting discounts and commissions to be paid by us	$	$	$

Proceeds, before expenses, to us	$	$	$

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 $. We have agreed to reimburse the underwriters $ 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

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, or SEC, a registration statement under the Securities Act of 1933, as amended, which we refer to as 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 75 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 75-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 75 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

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succession to the legal representative, heir, beneficiary or a member of the immediate family of the director or 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 Securities Exchange Act of 1934, as amended, which we refer to as 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 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 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 restricted period or any extension thereof pursuant to the lock-up agreement, (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 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 45th day after the date of this prospectus supplement and the 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 45 days after the date of this prospectus supplement and ending at the expiration of the 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.

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

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

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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.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, 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.

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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.

Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts, the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

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 (each, a Relevant Member State), the underwriters have represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, or the Relevant Implementation Date, it has not made and will not make an offer of the notes which are the subject of the offering contemplated by this prospectus supplement to the public in

that Relevant Member State other than:

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

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives for any such offer; or

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

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provided that no such offer of notes shall require us or the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer of notes to the public in relation to any notes 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 the notes to be offered so as to enable an investor to decide to purchase or subscribe the notes 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 (as amended, including by Directive 2010/73/EU), and includes any relevant implementing measure in the Relevant Member State.

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.

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

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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, 2015 and the effectiveness of Agios Pharmaceuticals, Inc. s internal control over financial reporting as of December 31, 2015 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon the reports 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 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, 2015, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2016 Annual Meeting of Stockholders;

- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2016 and June 30, 2016;

- Our Current Reports on Form 8-K dated January 11, 2016; February 5, 2016; February 8, 2016; April 14, 2016; April 22, 2016; May 23, 2016; June 13, 2016; June 22, 2016; August 16, 2016; and August 26, 2016; 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.

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.

88 Sidney Street

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 supplement or in any free writing prospectuses we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares of common stock offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained or incorporated by reference in this prospectus is current only as of its date.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the SEC, as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended, which we refer to as the Securities Act, utilizing an automatic shelf registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus and, accordingly, to the extent inconsistent, information in this prospectus is superseded by the information in the prospectus supplement or any related free writing prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading Where You Can Find More Information beginning on page 2 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or such accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

This prospectus does not contain all of the information included in the registration statement. The registration statement filed with the SEC includes or incorporates by reference exhibits that provide more details about the matters discussed in this prospectus. You should carefully read this prospectus, the related exhibits filed with the SEC and any prospectus supplement, together with the additional information described below under the headings Where You Can Find More Information and Incorporation by Reference.

THIS PROSPECTUS MAY NOT BE USED TO SELL ANY SECURITIES UNLESS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

No offer of these securities will be made in any jurisdiction where the offer is not permitted.

Unless the context otherwise indicates, references in this prospectus to we, our and us refer, collectively, to Agios Pharmaceuticals, Inc., a Delaware corporation, and its consolidated subsidiaries.

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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 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 is part of a registration statement we filed with the SEC. This prospectus omits 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 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.

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INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference 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 in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this 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 or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates 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 and December 8, 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.

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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FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements are based on current expectations, estimates, forecasts and projections about the industry in which we operate and the beliefs and assumptions of our management.

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.

You are cautioned that these forward-looking statements are only predictions and are subject to risks, uncertainties and assumptions that are referenced in the section of any accompanying prospectus supplement entitled Risk Factors. You should also carefully review the risk factors and cautionary statements described in the other documents we file from time to time with the SEC, specifically our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. We undertake no obligation to revise or update any forward-looking statements, except to the extent required by law.

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AGIOS PHARMACEUTICALS, INC.

We are a biopharmaceutical company committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and with rare genetic disorders of metabolism, which are a subset of orphan genetic metabolic diseases. Metabolism is a complex biological process involving the uptake and assimilation of nutrients in cells to produce energy and facilitate many of the processes required for cellular division and growth. We believe that dysregulation of normal cellular metabolism plays a crucial role in many diseases, including certain cancers and rare genetic disorders. We focus our efforts on using cellular metabolism, an unexploited area of biological research with disruptive potential, as a platform for developing potentially transformative small molecule medicines for cancer and rare genetic disorders.

We were incorporated under the laws of the State of Delaware in August 2007. Our principal 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 on our website is not incorporated by reference into this prospectus, and you should not consider any information contained on, or that can be accessed through, our website as part of this prospectus or in deciding whether to purchase our securities.

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CONSOLIDATED RATIOS OF EARNINGS TO FIXED CHARGES AND RATIOS OF EARNINGS TO COMBINED FIXED CHARGES AND PREFERRED STOCK DIVIDENDS

The following table sets forth our ratio of earnings to fixed charges and the ratio of earnings to combined fixed charges and preferred stock dividends for each of the periods indicated. You should read this table in conjunction with the consolidated financial statements and notes incorporated by reference in this prospectus.

	Nine Months Ended September 30,	Fiscal Year Ended December 31,		
	2014	2013	2012	2011
Consolidated ratios of earnings to fixed charges(1)(2)	N/A	N/A	N/A	N/A
Consolidated ratios of earnings to combined fixed charges and preferred stock dividends(1)(3)	N/A	N/A	N/A	N/A

1) Due to our losses for the nine months ended September 30, 2014 and for the years ended December 31, 2013, 2012, and 2011, the coverage ratio was less than 1:1.
2) We would have needed to generate additional earnings of $27.9 million, $38.3 million, $25.8 million and $9.4 million for the nine months ended September 30, 2014 and for the years ended December 31, 2013, 2012, and 2011, respectively, to cover our fixed charges in those periods.
3) We would have needed to generate additional earnings of $27.9 million, $42.5 million, $33.0 million and $12.5 million for the nine months ended September 30, 2014 and for the years ended December 31, 2013, 2012, and 2011, respectively, to cover our fixed charges and accrued preferred dividends during those periods. We did not have any preferred stock outstanding after the completion of our initial public offering in July 2013.

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RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks and uncertainties described under Risk Factors in our most recent Form 10-K and any subsequent Forms 10-Q, and in any accompanying prospectus supplement, together with all of the other information included or incorporated by reference in this prospectus and in any accompanying prospectus supplement, including our consolidated financial statements and related notes, before deciding whether to purchase our securities. Any of these risks could materially and adversely affect our business, operating results, financial condition, or prospects and cause the value of our securities to decline, which could cause you to lose all or part of your investment.

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USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include the acquisition of companies or businesses, repayment and refinancing of debt, working capital and capital expenditures. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

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DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to the senior debt securities and the subordinated debt securities collectively as debt securities. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered. When we refer to the Company, we, our, and us in this section, we mean Agios Pharmaceuticals, Inc. excluding, unless the context otherwise requires or as otherwise expressly stated, our subsidiaries.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information.

None of the indentures will limit the amount of debt securities that we may issue. The applicable indenture will provide that debt securities may be issued up to an aggregate principal amount authorized from time to time by us and may be payable in any currency or currency unit designated by us or in amounts determined by reference to an index.

General

The senior debt securities will constitute our unsecured and unsubordinated general obligations and will rank pari passu with our other unsecured and unsubordinated obligations. The subordinated debt securities will constitute our unsecured and subordinated general obligations and will be junior in right of payment to our senior indebtedness (including senior debt securities), as described under the heading Certain Terms of the Subordinated Debt Securities Subordination. The debt securities will be structurally subordinated to all existing and future indebtedness and other liabilities of our subsidiaries unless such subsidiaries expressly guarantee such debt securities.

The debt securities will be our unsecured obligations. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations.

The applicable prospectus supplement and/or free writing prospectus will include any additional or different terms of the debt securities of any series being offered, including the following terms:

- the title and type of the debt securities;

whether the debt securities will be senior or subordinated debt securities, and, with respect to debt securities issued under the subordinated indenture the terms on which they are subordinated;

the aggregate principal amount of the debt securities;

the price or prices at which we will sell the debt securities;

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the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;

the rate or rates, if any, per year, at which the debt securities will bear interest, or the method of determining such rate or rates;

the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the manner of determination of such interest payment dates and the related record dates;

the right, if any, to extend the interest payment periods and the duration of that extension;

the manner of paying principal and interest and the place or places where principal and interest will be payable;

provisions for a sinking fund, purchase fund or other analogous fund, if any;

any redemption dates, prices, obligations and restrictions on the debt securities;

the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;

any conversion or exchange features of the debt securities;

whether and upon what terms the debt securities may be defeased;

any events of default or covenants in addition to or in lieu of those set forth in the indenture;

whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;

whether the debt securities will be guaranteed as to payment or performance;

any special tax implications of the debt securities; and

any other material terms of the debt securities.

When we refer to principal in this section with reference to the debt securities, we are also referring to premium, if any.

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than (1) the payment of interest accruing prior to the issue date of such further debt securities or (2) the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement. We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities may bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount. U.S. federal income tax considerations applicable to any such discounted debt securities or to certain debt securities issued at par which are treated as having been issued at a discount for U.S. federal income tax purposes will be described in the applicable prospectus supplement.

We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange

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rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked and certain related tax considerations will be set forth in the applicable prospectus supplement.

Certain Terms of the Senior Debt Securities

Covenants. Unless we indicate otherwise in a prospectus supplement, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or any of our subsidiaries from incurring, issuing, assuming or guaranteeing any indebtedness secured by a lien on any of our or our subsidiaries property or capital stock, or restricting either us or any of our subsidiaries from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, in either case, unless:

- the successor entity, if any, is a U.S. corporation, limited liability company, partnership or trust (subject to certain exceptions provided for in the senior indenture);
- the successor entity assumes our obligations on the senior debt securities and under the senior indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- certain other conditions are met.

No Protection in the Event of a Change in Control. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any provisions that may afford holders of the senior debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

Events of Default. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the following are events of default under the senior indenture for any series of senior debt securities:

- failure to pay interest on any senior debt securities of such series when due and payable, if that default continues for a period of 30 days (or such other period as may be specified for such series);

failure to pay principal on the senior debt securities of such series when due and payable whether at maturity, upon redemption, by declaration or otherwise (and, if specified for such series, the continuance of such failure for a specified period);

default in the performance of or breach of any of our covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90 days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;

certain events of bankruptcy or insolvency, whether or not voluntary; and

any other event of default provided for in such series of senior debt securities as may be specified in the applicable prospectus supplement.

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The default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

If an event of default other than an event of default specified in the fourth bullet point above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest on such series of senior debt securities to be immediately due and payable, and upon this declaration, the same shall become immediately due and payable.

If an event of default specified in the fourth bullet point above occurs and is continuing, the entire principal amount of and accrued interest on each series of senior debt securities then outstanding shall become immediately due and payable.

Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by the default, each series voting as a separate class. Furthermore, subject to various provisions in the senior indenture, the holders of a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive an existing default or event of default with respect to such senior debt securities and its consequences, except a default in the payment of principal of or interest on such senior debt securities or in respect of a covenant or provision of the senior indenture which cannot be modified or amended without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto.

The holders of a majority in aggregate principal amount of a series of senior debt securities may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

- the holder gives the trustee written notice of a continuing event of default;

- the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;

the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;

the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and

during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

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These limitations, however, do not apply to the right of any holder of a senior debt security to receive payment of the principal of and interest on such senior debt security in accordance with the terms of such debt security, or to bring suit for the enforcement of any such payment in accordance with the terms of such debt security, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all covenants, agreements and conditions under the senior indenture.

Satisfaction and Discharge. We can satisfy and discharge our obligations to holders of any series of debt securities if:

- we pay or cause to be paid, as and when due and payable, the principal of and any interest on all senior debt securities of such series outstanding under the senior indenture; or

- all senior debt securities of such series have become due and payable or will become due and payable within one year (or are to be called for redemption within one year) and we deposit in trust a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us. Purchasers of the debt securities should consult their own advisers with respect to the tax consequences to them of such deposit and discharge, including the applicability and effect of tax laws other than the U.S. federal income tax law.

Defeasance. Unless the applicable prospectus supplement provides otherwise, the following discussion of legal defeasance and discharge and covenant defeasance will apply to any series of debt securities issued under the indentures.

Legal Defeasance. We can legally release ourselves from any payment or other obligations on the debt securities of any series (called legal defeasance) if certain conditions are met, including the following:

- We deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

- There is a change in current U.S. federal income tax law or an IRS ruling that lets us make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due. Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us.

We deliver to the trustee a legal opinion of our counsel confirming the tax law change or ruling described above.

If we accomplish legal defeasance, as described above, you would have to rely solely on the trust deposit for repayment of the debt securities. You could not look to us for repayment in the event of any shortfall.

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Covenant Defeasance. Without any change of current U.S. federal tax law, we can make the same type of deposit described above and be released from some of the covenants in the debt securities (called covenant defeasance). In that event, you would lose the protection of those covenants but would gain the protection of having money and securities set aside in trust to repay the debt securities. In order to achieve covenant defeasance, we must do the following (among other things):

We must deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

We must deliver to the trustee a legal opinion of our counsel confirming that under current U.S. federal income tax law we may make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due.

If we accomplish covenant defeasance, you could still look to us for repayment of the debt securities if there were a shortfall in the trust deposit. In fact, if one of the events of default occurred (such as our bankruptcy) and the debt securities become immediately due and payable, there may be such a shortfall. Depending on the events causing the default, you may not be able to obtain payment of the shortfall.

Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities without the consent of any holder:

to convey, transfer, assign, mortgage or pledge any assets as security for the senior debt securities of one or more series;

to evidence the succession of a corporation, limited liability company, partnership or trust to us, and the assumption by such successor of our covenants, agreements and obligations under the senior indenture or to otherwise comply with the covenant relating to mergers, consolidations and sales of assets;

to comply with requirements of the SEC in order to effect or maintain the qualification of the senior indenture under the Trust Indenture Act of 1939, as amended;

to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;

to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of senior debt securities of such series set forth in this prospectus or any applicable prospectus supplement;

to provide for or add guarantors with respect to the senior debt securities of any series;

to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;

to evidence and provide for the acceptance of appointment under the senior indenture by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;

to add to, delete from or revise the conditions, limitations and restrictions on the authorized amount, terms, purposes of issue, authentication and delivery of any series of senior debt securities;

to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding; or

to make any change that does not adversely affect the rights of any holder in any material respect.

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Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of a majority of the aggregate principal amount of the outstanding senior debt securities of all series affected by the amendment or modification (voting together as a single class); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

- extends the final maturity of any senior debt securities of such series;
- reduces the principal amount of any senior debt securities of such series;
- reduces the rate or extends the time of payment of interest on any senior debt securities of such series;
- reduces the amount payable upon the redemption of any senior debt securities of such series;
- changes the currency of payment of principal of or interest on any senior debt securities of such series;
- reduces the principal amount of original issue discount securities payable upon acceleration of maturity or the amount provable in bankruptcy;
- waives an uncured default in the payment of principal of or interest on the senior debt securities (except in the case of a rescission of acceleration as described above);
- changes the provisions relating to the waiver of past defaults or changes or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment or conversion of any senior debt securities of such series on or after the due date therefor;
- modifies any of the provisions of these restrictions on amendments and modifications, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification; or
- reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or modifies or amends or waives certain provisions of or defaults under the senior indenture.

It shall not be necessary for the holders to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if the holders consent approves the substance thereof. After an amendment, supplement or waiver of the senior indenture in accordance with the provisions described in this section becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment,

supplement or waiver. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such amendment, supplemental indenture or waiver.

No Personal Liability of Incorporators, Stockholders, Officers, Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of an event of default, the trustee will not be liable except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person s own affairs.

The senior indenture and the provisions of the Trust Indenture Act of 1939 incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or any of our

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subsidiaries, to obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claims, as security or otherwise. The trustee is permitted to engage in other transactions, provided that if it acquires any conflicting interest (as defined in the Trust Indenture Act), it must eliminate such conflict or resign.

We may have normal banking relationships with the senior trustee in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for two years after the date upon which such principal, premium or interest became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the senior debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities.

Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all of our senior indebtedness, as defined in the subordinated indenture. During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our senior indebtedness, we may not make any payment of principal of or interest on the subordinated debt securities (except for certain sinking fund payments). In addition, upon any payment or distribution of our assets upon any dissolution, winding-up, liquidation or reorganization, the payment of the principal of and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our senior indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our senior indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

The term senior indebtedness of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

all of the indebtedness of that person for money borrowed;

all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;

all of the lease obligations that are capitalized on the books of that person in accordance with generally accepted accounting principles;

all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and

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all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above;

unless, in the case of any particular indebtedness, renewal, extension or refunding, the instrument creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute senior indebtedness for purposes of the subordinated debt indenture.

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DESCRIPTION OF CAPITAL STOCK

General

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our certificate of incorporation, our by-laws and applicable provisions of Delaware corporate law. You should read our certificate of incorporation and by-laws, which are filed as exhibits to the registration statement of which this prospectus forms a part, for the provisions that are important to you.

Our authorized capital stock consists of 125,000,000 shares of common stock, par value $0.001 per share, and 25,000,000 shares of preferred stock, par value $0.001 per share. As of December 8, 2014, 34,749,064 shares of common stock were outstanding and no shares of preferred stock were outstanding.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Preferred Stock

We are authorized to issue blank check preferred stock, which may be issued in one or more series upon authorization of our board of directors. Our board of directors is authorized to fix the designation of the series, the number of authorized shares of the series, dividend rights and terms, conversion rights, voting rights, redemption rights and terms, liquidation preferences and any other rights, powers, preferences and limitations applicable to each series of preferred stock. The authorized shares of our preferred stock are available for issuance without further action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange on which our securities may be listed. If the approval of our stockholders is not required for the issuance of shares of our preferred stock, our board may determine not to seek stockholder approval. The specific terms of any series of preferred stock offered pursuant to this prospectus will be described in the prospectus supplement relating to that series of preferred stock.

A series of our preferred stock could, depending on the terms of such series, impede the completion of a merger, tender offer or other takeover attempt. Our board of directors will make any determination to issue preferred shares based upon its judgment as to the best interests of our stockholders. Our directors, in so acting, could issue preferred

stock having terms that could discourage an acquisition attempt through which an acquirer may be able to change the composition of our board of directors, including a tender offer or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over the then-current market price of the stock.

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The preferred stock has the terms described below unless otherwise provided in the prospectus supplement relating to a particular series of preferred stock. You should read the prospectus supplement relating to the particular series of preferred stock being offered for specific terms, including:

- the designation and stated value per share of the preferred stock and the number of shares offered;
- the amount of liquidation preference per share;
- the price at which the preferred stock will be issued;
- the dividend rate, or method of calculation of dividends, the dates on which dividends will be payable, whether dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends will commence to accumulate;
- any redemption or sinking fund provisions;
- if other than the currency of the United States, the currency or currencies including composite currencies in which the preferred stock is denominated and/or in which payments will or may be payable;
- any conversion provisions;
- any other rights, preferences, privileges, limitations and restrictions on the preferred stock.

The preferred stock will, when issued, be fully paid and non-assessable. Unless otherwise specified in the prospectus supplement, each series of preferred stock will rank equally as to dividends and liquidation rights in all respects with each other series of preferred stock. The rights of holders of shares of each series of preferred stock will be subordinate to those of our general creditors.

Rank. Unless otherwise specified in the prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon our liquidation, dissolution or winding up of our affairs, rank:

- senior to our common stock and to all equity securities ranking junior to such preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs;
- on a parity with all equity securities issued by us, the terms of which specifically provide that such equity securities rank on a parity with the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs; and

junior to all equity securities issued by us, the terms of which specifically provide that such equity securities rank senior to the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs.

The term equity securities does not include convertible debt securities.

Dividends. Holders of the preferred stock of each series will be entitled to receive, when, as and if declared by our board of directors, cash dividends at such rates and on such dates described in the prospectus supplement. Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

Dividends on any series of preferred stock may be cumulative or noncumulative, as described in the applicable prospectus supplement. If our board of directors does not declare a dividend payable on a dividend payment date on any series of noncumulative preferred stock, then the holders of that noncumulative preferred stock will have no right to receive a dividend for that dividend payment date, and we will have no obligation to pay the dividend accrued for that period, whether or not dividends on that series are declared payable on any future dividend payment dates. Dividends on any series of cumulative preferred stock will accrue from the date we initially issue shares of such series or such other date specified in the applicable prospectus supplement.

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No dividends may be declared or paid or funds set apart for the payment of any dividends on any parity securities unless full dividends have been paid or set apart for payment on the preferred stock. If full dividends are not paid, the preferred stock will share dividends pro rata with the parity securities.

No dividends may be declared or paid or funds set apart for the payment of dividends on any junior securities unless full dividends for all dividend periods terminating on or prior to the date of the declaration or payment will have been paid or declared and a sum sufficient for the payment set apart for payment on the preferred stock.

Liquidation Preference. Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, then, before we make any distribution or payment to the holders of any common stock or any other class or series of our capital stock ranking junior to the preferred stock in the distribution of assets upon any liquidation, dissolution or winding up of our affairs, the holders of each series of preferred stock shall be entitled to receive out of assets legally available for distribution to stockholders, liquidating distributions in the amount of the liquidation preference per share set forth in the prospectus supplement, plus any accrued and unpaid dividends thereon. Such dividends will not include any accumulation in respect of unpaid noncumulative dividends for prior dividend periods. Unless otherwise specified in the prospectus supplement, after payment of the full amount of their liquidating distributions, the holders of preferred stock will have no right or claim to any of our remaining assets. Upon any such voluntary or involuntary liquidation, dissolution or winding up, if our available assets are insufficient to pay the amount of the liquidating distributions on all outstanding preferred stock and the corresponding amounts payable on all other classes or series of our capital stock ranking on parity with the preferred stock and all other such classes or series of shares of capital stock ranking on parity with the preferred stock in the distribution of assets, then the holders of the preferred stock and all other such classes or series of capital stock will share ratably in any such distribution of assets in proportion to the full liquidating distributions to which they would otherwise be entitled.

Upon any such liquidation, dissolution or winding up and if we have made liquidating distributions in full to all holders of preferred stock, we will distribute our remaining assets among the holders of any other classes or series of capital stock ranking junior to the preferred stock according to their respective rights and preferences and, in each case, according to their respective number of shares. For such purposes, our consolidation or merger with or into any other corporation, trust or entity, or the sale, lease or conveyance of all or substantially all of our property or assets will not be deemed to constitute a liquidation, dissolution or winding up of our affairs.

Redemption. If so provided in the applicable prospectus supplement, the preferred stock will be subject to mandatory redemption or redemption at our option, as a whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in such prospectus supplement.

The prospectus supplement relating to a series of preferred stock that is subject to mandatory redemption will specify the number of shares of preferred stock that shall be redeemed by us in each year commencing after a date to be specified, at a redemption price per share to be specified, together with an amount equal to all accrued and unpaid dividends thereon to the date of redemption. Unless the shares have a cumulative dividend, such accrued dividends will not include any accumulation in respect of unpaid dividends for prior dividend periods. We may pay the redemption price in cash or other property, as specified in the applicable prospectus supplement. If the redemption price for preferred stock of any series is payable only from the net proceeds of the issuance of shares of our capital stock, the terms of such preferred stock may provide that, if no such shares of our capital stock shall have been issued or to the extent the net proceeds from any issuance are insufficient to pay in full the aggregate redemption price then due, such preferred stock shall automatically and mandatorily be converted into the applicable shares of our capital stock pursuant to conversion provisions specified in the applicable prospectus supplement. Notwithstanding the foregoing, we will not redeem any preferred stock of a series unless:

if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on the preferred stock for all past dividend periods and the then current dividend period; or

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if such series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends for the then current dividend period.

In addition, we will not acquire any preferred stock of a series unless:

if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on all outstanding shares of such series of preferred stock for all past dividend periods and the then current dividend period; or

if that series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends on the preferred stock of such series for the then current dividend period.

However, at any time we may purchase or acquire preferred stock of that series (1) pursuant to a purchase or exchange offer made on the same terms to holders of all outstanding preferred stock of such series or (2) by conversion into or exchange for shares of our capital stock ranking junior to the preferred stock of such series as to dividends and upon liquidation.

If fewer than all of the outstanding shares of preferred stock of any series are to be redeemed, we will determine the number of shares that may be redeemed pro rata from the holders of record of such shares in proportion to the number of such shares held or for which redemption is requested by such holder or by any other equitable manner that we determine. Such determination will reflect adjustments to avoid redemption of fractional shares.

Unless otherwise specified in the prospectus supplement, we will mail notice of redemption at least 30 days but not more than 60 days before the redemption date to each holder of record of preferred stock to be redeemed at the address shown on our stock transfer books. Each notice shall state:

the redemption date;

the number of shares and series of preferred stock to be redeemed;

the redemption price;

the place or places where certificates for such preferred stock are to be surrendered for payment of the redemption price;

that dividends on the shares to be redeemed will cease to accrue on such redemption date;

the date on which the holder s conversion rights, if any, as to such shares shall terminate; and

the specific number of shares to be redeemed from each such holder if fewer than all the shares of any series are to be redeemed.

If notice of redemption has been given and we have set aside the funds necessary for such redemption in trust for the benefit of the holders of any shares called for redemption, then from and after the redemption date, dividends will cease to accrue on such shares, and all rights of the holders of such shares will terminate, except the right to receive the redemption price.

Voting Rights. Holders of preferred stock will not have any voting rights, except as required by law or as indicated in the applicable prospectus supplement.

Unless otherwise provided for under the terms of any series of preferred stock, no consent or vote of the holders of shares of preferred stock or any series thereof shall be required for any amendment to our certificate of incorporation that would increase the number of authorized shares of preferred stock or the number of authorized

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shares of any series thereof or decrease the number of authorized shares of preferred stock or the number of authorized shares of any series thereof (but not below the number of authorized shares of preferred stock or such series, as the case may be, then outstanding).

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into our common stock will be set forth in the applicable prospectus supplement relating thereto. Such terms will include the number of shares of common stock into which the shares of preferred stock are convertible, the conversion price, rate or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or at the option of the holders of the preferred stock, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption.

Transfer Agent and Registrar. The transfer agent and registrar for the preferred stock will be set forth in the applicable prospectus supplement.

Registration Rights

We have entered into a second amended and restated investor rights agreement, dated November 16, 2011, which we refer to as the investor rights agreement, with certain holders of our common stock. These holders have the right to require us to register under the Securities Act certain shares they acquired in private placements prior to our initial public offering, and to participate in future registrations of securities by us, under the circumstances described below. In addition, an affiliate of Celgene also has these same registration rights with respect to shares of our common stock acquired in our July 2013 private placement. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. If not otherwise exercised, the rights described below will expire in July 2018, which is five years after the closing of our initial public offering.

Demand Registration Rights

Beginning January 24, 2014, subject to specified limitations set forth in the investor rights agreement, at any time, the holders of a majority of the then outstanding shares having rights under the investor rights agreement, which we refer to as registrable shares, may at any time demand in writing that we register all or a portion of the registrable shares under the Securities Act if the total amount of registrable shares registered have an aggregate offering price of at least $5 million (based on the then current market price). We are not obligated to file a registration statement pursuant to this provision on more than two occasions.

In addition, subject to specified limitations set forth in the investor rights agreement, at any time after we become eligible to file a registration statement on Form S-3, holders of at least 25% of the registrable shares then outstanding may request that we register their registrable securities on Form S-3 for purposes of a public offering if the total amount of registrable shares registered have an aggregate offering price of at least $5 million (based on the then current market price). We are not obligated to file a registration statement pursuant to this provision on more than two occasions in any 12-month period.

Incidental Registration Rights

If we propose to file a registration statement to register any of our securities under the Securities Act, either for our own account or for the account of any of our stockholders, other than pursuant to the demand registration rights described above and other than pursuant to a Form S-4 or Form S-8, the holders of our registrable securities are entitled to notice of registration and, subject to specified exceptions, we will be required upon the holder s request to use our best efforts to register their then held registrable securities.

In the event that any registration in which the holders of registrable shares participate pursuant to our investor rights agreement is an underwritten public offering, we agree to enter into an underwriting agreement containing customary representation and warranties and covenants, including without limitation customary provisions with respect to indemnification of the underwriters of such offering.

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In the event that any registration in which the holders of registrable shares participate pursuant to our investor rights agreement is an underwritten public offering, we will use our best efforts to include the requested registrable shares to be included, but may be limited by market conditions.

Expenses

Pursuant to the investor rights agreement, we are required to pay all registration and filing fees, exchange listing fees, printing expenses, fees and expenses of one counsel to represent the selling stockholders, state Blue Sky fees and expenses, and the expense of any special audits incident to or required by any such registration, but excluding underwriting discounts, selling commissions and the fees and expenses of selling stockholders own counsel (other than the counsel selected to represent all selling stockholders). We are not required to pay registration expenses if a demand registration request under the investor rights agreement is withdrawn at the request of holders who exercise their demand right to register the registrable securities, unless the withdrawal is due to discovery of a materially adverse change in our business.

The investor rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Provisions of Our Certificate of Incorporation and By-laws and Delaware Law That May Have Anti-Takeover Effects

The provisions of Delaware law and our certificate of incorporation and by-laws could discourage or make it more difficult to accomplish a proxy contest or other change in our management or the acquisition of control by a holder of a substantial amount of our voting stock. It is possible that these provisions could make it more difficult to accomplish, or could deter, transactions that stockholders may otherwise consider to be in their best interests or in our best interests. These provisions are intended to enhance the likelihood of continuity and stability in the composition of our board of directors and in the policies formulated by the board of directors and to discourage certain types of transactions that may involve an actual or threatened change of our control. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal and to discourage certain tactics that may be used in proxy fights. Such provisions also may have the effect of preventing changes in our management.

Delaware Business Combination Statute. Section 203 of the General Corporation Law of the State of Delaware, which we refer to as the DGCL, is applicable to us. Section 203 of the DGCL restricts some types of transactions and business combinations between a corporation and a 15% stockholder. A 15% stockholder is generally considered by Section 203 to be a person owning 15% or more of the corporation s outstanding voting stock. Section 203 refers to a 15% stockholder as an interested stockholder. Section 203 restricts these transactions for a period of three years from the date the stockholder acquires 15% or more of our outstanding voting stock. With some exceptions, unless the transaction is approved by the board of directors and the holders of at least two-thirds of the outstanding voting stock of the corporation, Section 203 prohibits significant business transactions such as:

- a merger with, disposition of significant assets to or receipt of disproportionate financial benefits by the interested stockholder, and

any other transaction that would increase the interested stockholder s proportionate ownership of any class or series of our capital stock.

The shares held by the interested stockholder are not counted as outstanding when calculating the two-thirds of the outstanding voting stock needed for approval.

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The prohibition against these transactions does not apply if:

- prior to the time that any stockholder became an interested stockholder, the board of directors approved either the business combination or the transaction in which such stockholder acquired 15% or more of our outstanding voting stock, or

- the interested stockholder owns at least 85% of our outstanding voting stock as a result of a transaction in which such stockholder acquired 15% or more of our outstanding voting stock. Shares held by persons who are both directors and officers or by some types of employee stock plans are not counted as outstanding when making this calculation.

Board of Directors. Our certificate of incorporation and by-laws provide for a board of directors divided as nearly equally as possible into three classes. Each class is elected to a term expiring at the annual meeting of stockholders held in the third year following the year of such election. Under our certificate of incorporation and bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors.

Removal of Directors by Stockholders. Our certificate of incorporation and bylaws provide that a director may be removed only for cause and only by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors.

Super Majority Stockholder Vote Required for Certain Actions. The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation s certificate of incorporation or by-laws, unless a corporation s certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our by-laws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes which all our stockholders would be entitled to cast in an election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described in this section of the prospectus entitled Provisions of Our Certificate of Incorporation and By-laws and Delaware Law That May Have Anti-Takeover Effects.

Advance Notice Provisions for Stockholder Proposals and Stockholder Nomination of Directors. Our by-laws provide that, for nominations to the board of directors or for other business to be properly brought by a stockholder before a meeting of stockholders, a stockholder must first have given timely notice of the proposal in writing to our secretary. Our certificate of incorporation and bylaws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our chairman of the board, our chief executive officer or our board of directors. In addition, our bylaws provide that, for an annual meeting, a stockholder notice generally must be delivered not earlier than the 120th day and not later than the 90th day prior to the first anniversary of the preceding year s annual meeting; provided, that if the date of the annual meeting is advanced by more than 20 days or delayed by more than 60 days from such anniversary date, notice by the stockholder to be timely must be so delivered not earlier than the 120th day prior to the date of such annual meeting and not later than the close of business on the later of the 90th day prior to the date of such meeting and the 10th day following the day on which public announcement of the date of such annual meeting is first made by us. For a special meeting, such notice must be delivered not earlier than the 120th day prior to such special meeting and not later than the close of business on the later of (x) the 90th day prior to such

special meeting and (y) the 10th day following the day on which notice of the date of such special meeting was mailed or public disclosure of the date of such special meeting was made, whichever first occurs. Detailed requirements as to the form of the notice and information required in the notice are specified in our by-laws.

No Action By Written Consent. Our certificate of incorporation provides that our stockholders may not act by written consent and may only act at duly called meetings of stockholders.

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DESCRIPTION OF WARRANTS

We may issue warrants to purchase common stock, preferred stock or debt securities. We may offer warrants separately or together with one or more additional warrants, common stock, preferred stock or debt securities, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;

if applicable, the designation and terms of the preferred stock with which the warrants are issued and the number of warrants issued with each security;

if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, preferred stock or common stock will be separately transferable;

the number of shares of common stock, preferred stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

information with respect to book-entry procedures, if any;

the anti-dilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;

any redemption or call provisions; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

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FORMS OF SECURITIES

Each debt security and warrant will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depositary or its nominee as the owner of the debt securities or warrants represented by these global securities. The depositary maintains a computerized system that will reflect each investor s beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the debt securities and warrants in the form of one or more fully registered global securities that will be deposited with a depositary or its nominee identified in the applicable prospectus supplement and registered in the name of that depositary or nominee. In those cases, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a global security may not be transferred except as a whole by and among the depositary for the global security, the nominees of the depositary or any successors of the depositary or those nominees.

If not described below, any specific terms of the depositary arrangement with respect to any securities to be represented by a global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depositary arrangements.

Ownership of beneficial interests in a global security will be limited to persons, called participants, that have accounts with the depositary or persons that may hold interests through participants. Upon the issuance of a global security, the depositary will credit, on its book-entry registration and transfer system, the participants accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depositary, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in global securities.

So long as the depositary, or its nominee, is the registered owner of a global security, that depositary or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the global security for all purposes under the applicable indenture or warrant agreement. Except as described below, owners of beneficial interests in a global security will not be entitled to have the securities represented by the global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture or warrant agreement. Accordingly, each person owning a beneficial interest in a global security must rely on the procedures of the depositary for that global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture or warrant agreement. We understand that under existing industry practices, if we request any action of holders or if an owner of

a beneficial interest in a global security desires to give or take any action that a holder is entitled to give or take under the applicable indenture or warrant

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agreement, the depositary for the global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to warrants, represented by a global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the global security. None of us, or any trustee, warrant agent, unit agent or other agent of ours, or any agent of any trustee, warrant agent or unit agent will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants accounts in amounts proportionate to their respective beneficial interests in that global security as shown on the records of the depositary. We also expect that payments by participants to owners of beneficial interests in a global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in street name, and will be the responsibility of those participants.

If the depositary for any of the securities represented by a global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the global security that had been held by the depositary. Any securities issued in definitive form in exchange for a global security will be registered in the name or names that the depositary gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depositary s instructions will be based upon directions received by the depositary from participants with respect to ownership of beneficial interests in the global security that had been held by the depositary.

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PLAN OF DISTRIBUTION

We may sell securities:

through underwriters;

through dealers;

through agents;

directly to purchasers; or

through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis.

The distribution of the securities may be effected from time to time in one or more transactions:

at a fixed price, or prices, which may be changed from time to time;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

the name of the agent or any underwriters;

the public offering or purchase price and the proceeds we will receive from the sale of the securities;

any discounts and commissions to be allowed or re-allowed or paid to the agent or underwriters;

all other items constituting underwriting compensation;

any discounts and commissions to be allowed or re-allowed or paid to dealers; and

any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which this prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

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If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Remarketing firms, agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in three business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than three scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the third

business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle more than three scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

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The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the aggregate maximum discount, commission or agency fees or other items constituting underwriting compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the proceeds from any offering pursuant to this prospectus and any applicable prospectus supplement.

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LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Wilmer Cutler Pickering Hale and Dorr LLP. Any underwriters will also be advised about legal matters by their own counsel, which will be named in the applicable prospectus supplement.

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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December 9, 2014

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