AGIOS PHARMACEUTICALS INC
Form 424B5
January 19, 2018
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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-221960

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered[1]	Proposed maximum offering price per unit	Proposed maximum aggregate offering price[1]	Amount of registration fee[2]
Common Stock, par value $0.001 per share	8,152,986	$67.00	$546,250,062	$68,009

(1) Assumes exercise in full of the underwriters option to purchase up to 1,063,433 additional shares of Common Stock.

(2) Calculated in accordance with Rule 457(r) under the Securities Act of 1933, as amended. This Calculation of Registration Fee table shall be deemed to update the Calculation of Registration Fee table in the registrant s Registration Statement on Form S-3 (File No. 333-221960) in accordance with Rules 456(b) and 457(r) under the Securities Act of 1933, as amended.

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Prospectus supplement

(To Prospectus dated December 8, 2017)

7,089,553 Shares

Common Stock

Agios Pharmaceuticals, Inc. is offering 7,089,553 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 January 18, 2018 was $68.15 per share.

Investing in our common stock involves risks. See Risk factors beginning on page S-21 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	$ 67.000	$ 475,000,051
Underwriting discounts(1)	$ 3.685	$ 26,125,003
Proceeds, before expenses, to Agios Pharmaceuticals, Inc.	$ 63.315	$ 448,875,048

(1) We have agreed to reimburse the underwriters for certain FINRA-related expenses. See Underwriting beginning on page S-33 of this prospectus supplement.

We have granted the underwriters the right to purchase up to an additional 1,063,433 shares of our common stock at the public offering price less the underwriting discounts and commissions. The underwriters can exercise this right at any time within 30 days after the date of this prospectus supplement.

Celgene Corporation, or Celgene, an existing stockholder and our strategic alliance partner in the fields of cancer metabolism and metabolic immuno-oncology, has indicated an interest in purchasing an aggregate of 851,154 shares of our common stock in this offering at the public offering price. However, because an indication of interest is not a binding agreement or commitment to purchase, Celgene may determine to purchase fewer shares than it has indicated

an interest in purchasing or not to purchase any shares in this offering. In addition, the underwriters could determine to sell fewer shares to Celgene than Celgene indicated an interest in purchasing or not to sell any shares to Celgene. The underwriters will receive the same underwriting discount on any shares purchased by Celgene as they will on any other shares sold to the public in this offering. Any shares sold to Celgene will be subject to the lock-up agreement described under Underwriting.

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

The underwriters expect to deliver the shares of common stock to investors on or about January 23, 2018.

Joint Book-Running Managers

J.P. Morgan **Goldman Sachs & Co. LLC** **Cowen**

Lead Managers

RBC Capital Markets **SunTrust Robinson Humphrey**

The date of this prospectus supplement is January 18, 2018.

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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-21 and the risk factors contained in our Annual Report on Form 10-K for the year ended December 31, 2016 and our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2017.

Overview

We are a biopharmaceutical company committed to the fundamental transformation of patients lives through scientific leadership in the field of cellular metabolism, with the goal of making transformative, first- or best-in-class medicines. Our therapeutic areas of focus are cancer and rare genetic diseases, or RGDs, which are diseases that are directly caused by changes in genes or chromosomes, often passed from one generation to the next. Most RGDs are often associated with severe or life-threatening features. The incidence of a single RGD can vary widely but is generally very infrequent, usually equal to or less than one per 100,000 births. In both areas of cancer and RGDs, we are seeking to unlock the biology of cellular metabolism as a platform to create transformative therapies.

Our first commercial cancer product is IDHIFA®. On August 1, 2017, the U.S. Food and Drug Administration, or FDA, granted our collaboration partner Celgene Corporation, or Celgene, approval of IDHIFA® for the treatment of adult patients with relapsed or refractory acute myeloid leukemia, or R/R AML, and an isocitrate dehydrogenase 2, or IDH2, mutation as detected by an FDA-approved test. IDHIFA®, an oral targeted inhibitor of the mutated IDH2 enzyme, is the first and only FDA-approved therapy for patients with R/R AML and an IDH2 mutation.

Our most advanced clinical cancer product candidates are ivosidenib, which targets mutated isocitrate dehydrogenase 1, or IDH1, and AG-881, which is a brain-penetrant pan-IDH inhibitor. These mutations are found in a wide range of cancers. In December 2017, we submitted a new drug application, or NDA, to the FDA for ivosidenib for the treatment of patients with R/R AML and an IDH1 mutation. We plan to submit a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, for ivosidenib for IDH1 mutant-positive R/R AML in the fourth quarter of 2018.

Our next most advanced cancer product candidate is AG-270, an inhibitor of methionine adenosyltransferase 2a, or MAT2A. We submitted an investigational new drug application, or IND, for AG-270 in November 2017 and in December 2017 the FDA concluded that we may proceed with our planned phase 1 dose-escalation trial of AG-270 in multiple tumor types carrying a methylthioadenosine phosphorylase, or MTAP, deletion. We expect to initiate this trial in the first quarter of 2018.

Our most advanced preclinical cancer product candidate is an inhibitor of the metabolic enzyme dihydroorotate dehydrogenase, or DHODH. We plan to submit an IND for our DHODH inhibitor for the treatment of hematologic malignancies in the fourth quarter of 2018.

The lead product candidate in our RGD program, AG-348, targets pyruvate kinase-R for the treatment of pyruvate kinase, or PK, deficiency. Pyruvate kinase deficiency is a rare genetic disorder that often results in severe hemolytic anemia, jaundice and lifelong conditions associated with chronic anemia and secondary complications 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. In December 2017,

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at the 2017 American Society of Hematology Annual Meeting and Exposition in Atlanta, Georgia, or ASH 2017, we presented updated clinical data from DRIVE PK demonstrating clinically meaningful, rapid and sustained hemoglobin, or Hb, increases in patients on the trial. We intend to initiate two global, pivotal trials of AG-348 in PK deficiency in the first half of 2018: ACTIVATE-T, a single arm trial of approximately 20 regularly transfused patients, is expected to initiate in the first quarter of 2018, and ACTIVATE, a 1:1 randomized, placebo-controlled trial of approximately 80 patients who do not receive regular transfusions, is expected to initiate in the second quarter of 2018. We also expect to initiate a phase 2 proof of concept trial of AG-348 in thalassemia in the fourth quarter of 2018.

In addition to the aforementioned development programs, we are seeking to advance a number of early-stage discovery programs in the areas of cancer metabolism, RGDs and metabolic immuno-oncology, or MIO, a developing field which aims to modulate the activity of relevant immune cells by targeting critical metabolic nodes, thereby, enhancing the immune mediated anti-tumor response.

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 with a focus in the field of cellular metabolism by building a research platform in cancer metabolism, RGDs and MIO.
- Collaborating closely with the FDA and other regulatory bodies to aggressively pursue early registration potential for our product candidates, for example by utilizing a similar regulatory path for ivosidenib as Celgene did for IDHIFA®.
- Continuing to build a product engine for cancer and RGDs to generate novel and important medicines.
- Building a preeminent and fully integrated independent biopharmaceutical company by engaging in discovery, development and commercialization of our medicines.
- Maintaining a commitment to precision medicine in drug development.

Our guiding principles

We aim to build a long-term company with a disciplined focus on developing medicines that transform the lives of patients with cancer and 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 a 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.

Our programs

Targeting mutated 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.

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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-hydroxyglutarate, or 2HG. We have shown 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 have shown that inhibition of these mutated proteins could lead to clinical benefit for the subset of cancer patients whose tumors carry these mutations. By reducing elevated 2HG levels, our IDH mutant inhibitors allow tumorous cells to undertake normal cellular differentiation and return to normally functioning cells in patients with acute myeloid leukemia, or AML. We estimate that there are approximately 10,000 AML patients in the United States and the European Union with IDH mutations, which we estimate has the potential to be an approximately $2 billion commercial opportunity. We have identified selective development candidates that separately target and inhibit the mutated forms of IDH1 and IDH2. To date, our clinical data with IDHIFA® and ivosidenib, our lead inhibitors of mutant IDH2 and IDH1, respectively, demonstrate evidence of cellular differentiation, normalization of cell counts and mutational clearance in the bone marrow and blood, a mechanism of response that is consistent with preclinical studies, including substantial reduction of plasma 2HG levels. This targeted differentiation effect is distinct from that seen with traditional cytotoxic chemotherapeutics, which lead to cell death, commonly used to treat cancer. Our goal is to establish our IDH mutation inhibitors as a cornerstone of AML therapy spanning all treatment lines.

IDHIFA®

IDHIFA® 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, who have a historically poor prognosis. On August 1, 2017, the FDA granted Celgene approval of IDHIFA® for the treatment of adult patients with R/R AML and an IDH2 mutation as detected by an FDA-approved test.

Celgene maintains worldwide development and commercial rights to IDHIFA® and will fund the future development and commercialization costs related to this program. Under the 2010 agreement described below, Celgene is responsible for all development costs for IDHIFA®, and we are eligible to receive up to $95 million in milestone payments, which are comprised of: (i) up to $70 million in milestone payments upon achievement of specified ex-U.S. regulatory milestone events and (ii) a $25 million milestone payment upon achievement of a specified commercial milestone event. Additionally, we are eligible to receive tiered royalties on any net sales of IDHIFA®. In January 2016, we earned a $25 million milestone payment upon initiation of the IDHENTIFY clinical trial, as described below. In addition to contributing our scientific and translational expertise, we will continue to conduct some clinical development and regulatory activities within the IDHIFA® development program under the 2010 agreement. We also have co-commercialization rights to provide up to one third of the field-based commercialization efforts and will be reimbursed for those efforts.

We continue to evaluate IDHIFA® in clinical trials evaluating hematological cancers with IDH2 mutations, which are led and funded by Celgene. To date, all clinical data reported by us and our collaborators in hematological cancers highlight that the mechanism of response is consistent with preclinical studies, including substantial reduction of plasma 2-hydroxygluturate, or 2HG, levels, as well as evidence of cellular differentiation and normalization of cell counts in the bone marrow and blood. This differentiation effect is distinct from that seen with traditional chemotherapeutics commonly used to treat AML. The FDA has granted orphan drug designation for IDHIFA® for treatment of patients with AML and fast track designation for treatment of patients with AML that harbor an IDH2 mutation, and the European Medicines Agency, or EMA, granted orphan drug designation for IDHIFA® for the treatment of AML.

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We and Celgene are evaluating IDHIFA® in the following clinical trials:

Phase 1/2 clinical trial

The FDA s approval of IDHIFA® in R/R AML was based on clinical data from an open-label, single-arm, multicenter, two-cohort phase 1/2 clinical trial of adult patients with R/R AML and an IDH2 mutation. The safety of IDHIFA® was evaluated in 214 patients in this trial. The median duration of exposure to IDHIFA® was 4.3 months (range 0.3 to 23.6). The 30 and 60-day mortality rates observed with IDHIFA® were 4.2% (9 of 214 patients) and 11.7% (25 of 214 patients), respectively. In the clinical trial, 14% of patients treated with IDHIFA® experienced differentiation syndrome, which can be fatal if not treated. The most common AEs seen in greater 20% of patients were nausea, vomiting, diarrhea, elevated bilirubin and decreased appetite. Serious adverse events, or SAEs, were reported in 77.1% of patients. The most frequent serious adverse reactions (greater than 2% of patients) were leukocytosis, diarrhea, nausea, vomiting, decreased appetite, tumor lysis syndrome, and differentiation syndrome. More than half (52%) of the treated patients were refractory to previous therapy. The efficacy of IDHIFA® was evaluated in 199 adult patients in the clinical trial. IDHIFA® was given orally at a starting dose of 100 mg daily until disease progression or unacceptable toxicity. Dose reductions were allowed to manage side effects. Patients had a median age of 68 years (range of 19 to 100) and received a median of two prior anticancer regimens (ranging from one to six). IDHIFA® demonstrated a combined CR or complete response with partial hematologic improvement, or CRh, rate of 23% (n=46) (95% CI: 18%, 30%). Median duration of CR/CRh was 8.2 months (95% CI: range 4.3, 19.4). For patients who achieved a CR/CRh, the median time to first response was 1.9 months (range, 0.5 to 7.5 months) and the median time to best response of CR/CRh was 3.7 months (range, 0.6 to 11.2 months). Of patients achieving a CR/CRh, 85% (39 of 46 patients) did so within six months of initiating IDHIFA®. 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. CRh is defined as less than 5% of blasts in the bone marrow, no evidence of disease and partial recovery of peripheral blood counts (platelets >50,000/lL and ANC >500/lL). Among the 157 patients who were dependent on red blood cell and/or platelet transfusions at baseline, 53 (34%) became independent of red blood cell and platelet transfusions during any 56-day post-baseline period. Of the 42 patients who were independent of both red blood cell and platelet transfusions at baseline, 32 (76%) remained transfusion independent during any 56-day post-baseline period.

Phase 1b frontline combination trial

IDHIFA® is being evaluated in a phase 1b, multicenter, international, open-label clinical trial, conducted by us, to evaluate the safety and clinical activity of IDHIFA® or ivosidenib 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 is evaluating continuous dosing for up to one year with IDHIFA® administered at an initial oral dose of 100 mg once daily in patients with an IDH2 mutation or ivosidenib administered at an initial oral dose of 500 mg once daily in patients with an IDH1 mutation. IDHIFA® or ivosidenib is 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). The trial is currently enrolling patients.

In December 2017, we presented interim data from this trial at ASH 2017. As of the August 1, 2017 data cut-off, in the IDHIFA® arm, the most common grade 3 or higher non-hematologic AEs during the induction period were febrile neutropenia (63%), blood bilirubin increase (9%), hypertension (9%) and bacteremia (9%). The 30 and 60-day mortality rates were 5% and 7%, respectively. There was one dose-limiting toxicity in the IDHIFA® arm consisting of persistent Grade 4 thrombocytopenia lasting beyond 42 days from the start of induction. The median time to absolute neutrophil count, or ANC, recovery (greater than 500/μL) was 34 days (95% CI 29,35). The median time to platelet recovery (greater than 50,000/μL) was 33 days (95% CI 29,50). In the IDHIFA® arm the overall best response rate of

combined CR and CRi/CRp, was 62% (31 of 50 response-evaluable patients); among 27 response-evaluable patients with de novo AML, the overall best response rate of combined CR and

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CRi/CRp was 67% (18 of 27 patients); and among 23 response-evaluable patients with secondary AML, the overall best response rate of combined CR and CRi/CRp was 57% (13 of 23 patients). A CRp, or complete remission with incomplete platelet recovery, means all the criteria for CR are met except that platelet counts are outside of the normal range. Platelets are one of the three major types of blood cells. A CRi, or complete remission with incomplete neutrophil or platelet recovery, 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. The interim reported results from the ivosidenib arm of this trial are discussed below under *Ivosidenib Phase 1(b) frontline combination trial*.

Phase 1/2 frontline combination trial

IDHIFA® is being evaluated in a phase 1/2 frontline combination clinical trial, conducted by Celgene, of either IDHIFA® or ivosidenib 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 the IDHIFA® investigational combination versus single-agent VIDAZA® using a primary endpoint of overall response rate. In the phase 1 component of the trial, patients received 100 mg (n=3) or 200 mg (n=3) of IDHIFA® daily plus VIDAZA® or 500 mg of ivosidenib (n=11) plus VIDAZA®. The trial has completed the phase 1 component and is currently enrolling in the phase 2 component.

In December 2017, we presented interim data from this trial at ASH 2017. As of the September 1, 2017 data cut-off, the median age of patients treated in the IDHIFA® arm was 68 (five out of six patients were 65 years old or older), and the most common grade 3-4 hematologic AE was neutropenia (33%), with thrombocytopenia, febrile neutropenia, anemia, lymphocyte count decreased and white blood cell count decreased all with one event (17% each), and the most common grade 3-4 non-hematologic AEs were pneumonia (33%) and hyperbilirubinemia (33%). IDH differentiation syndrome was reported in one patient. In the IDHIFA® arm, four of six patients had a response, including two CRs, one partial remission, or PR, and one morphologic leukemia-free state, or MLFS. 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. The interim reported results from the ivosidenib arm of this trial are discussed below under *Ivosidenib Phase 1/2 frontline combination trial*.

IDHENTIFY

IDHIFA® is being evaluated in IDHENTIFY, an international phase 3, multi-center, open-label, randomized clinical trial designed to compare the efficacy and safety of IDHIFA® versus conventional care regimens in patients 60 years or older with IDH2 mutant-positive AML that is refractory to or relapsed after second- or third-line therapy. In January 2016, in conjunction with the initiation of the IDHENTIFY clinical trial, we received a milestone payment of $25 million from Celgene pursuant to the 2010 agreement. This trial is currently enrolling patients and we have not yet presented any clinical data from this trial.

Phase 3 frontline combination trial

We plan to support, with Celgene, the initiation of an intergroup sponsored, global, registration-enabling phase 3 trial combining ivosidenib or IDHIFA® and standard induction (7+3) and consolidation chemotherapy with a primary endpoint of event free survival in frontline AML patients with an IDH1 or IDH2 mutation in the fourth quarter of 2018. The trial is expected to enroll approximately 500 patients with an IDH1 mutation and approximately 500 patients with an IDH2 mutation.

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Ivosidenib

Ivosidenib is our wholly owned, 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, cholangiocarcinoma and glioma where both the treatment options and prognosis for patients are poor. The FDA has granted us fast track designation to ivosidenib for treatment of patients with AML that harbor an IDH1 mutation and orphan drug designation for ivosidenib for treatment of patients with AML. The FDA has also granted fast-track designation to ivosidenib for treatment of patients with previously treated, unresectable or metastatic cholangiocarcinoma with and IDH1 mutation. In December 2017, we submitted an NDA to the FDA for ivosidenib for the treatment of patients with R/R AML and an IDH1 mutation. We plan to submit an MAA to the EMA for ivosidenib for IDH1 mutant-positive R/R AML in the fourth quarter of 2018.

We are evaluating ivosidenib in the following clinical trials:

Phase 1 clinical trial (advanced hematologic malignancies)

Ivosidenib is being evaluated in a phase 1 multicenter, open-label, dose-escalation and expansion clinical trial, designed to assess its safety, clinical activity and tolerability as a single agent in patients with advanced hematologic malignancies with an IDH1 mutation. Four expansion cohorts have been added to the trial. The first cohort is evaluating 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 is evaluating 25 untreated AML patients. The third cohort is evaluating 25 patients with other non-AML IDH1 mutant-positive relapsed or refractory advanced hematologic malignancies. The fourth cohort is evaluating patients with relapsed IDH1 mutant-positive AML not eligible for the first arm or standard of care chemotherapy. Ivosidenib is administered at a 500 mg once daily oral dose, in 28-day cycles. Enrollment to the trial is closed.

In December 2017, we presented interim clinical data from 258 patients treated with ivosidenib in the dose escalation and expansion arms of the trial at ASH 2017. Doses were administered from 200 mg to 1,200 mg total daily doses in dose escalation and 500 mg daily in dose expansion. A maximum tolerated dose, or MTD, was not reached in the dose escalation portion of the trial. As of the May 12, 2017 data cut-off, a safety analysis conducted for all 258 treated patients showed that ivosidenib continues to demonstrate a favorable safety profile. The most common AEs regardless of causality were diarrhea (33.3%), leukocytosis (30.2%), nausea (29.5%), fatigue (28.7%) and febrile neutropenia (25.2%). The data included 125 R/R AML patients who were enrolled at least six months prior to the data-cutoff, comprised of 92 patients from arm 1 of the expansion and 33 patients from the dose-escalation who met the eligibility criteria for arm 1 and received ivosidenib at 500 mg once daily. Among these 125 R/R AML patients, 8% reported grade ³3 leukocytosis, which was managed with hydroxyurea (no cases were fatal), 8% reported grade 3 QT prolongation (ivosidenib was reduced in one patient, and no cases were grade 4 or fatal), and 9.6% reported IDH differentiation syndrome, which was managed with corticosteroids and diuretics (no cases were grade 4 or fatal). Data from 125 R/R AML patients demonstrated a combined CR and CRh rate of 30.4% (95% CI 22.5, 39.3), which is the primary endpoint of the study. The CR rate was 21.6% (27 of 125 patients) (95% CI 14.7, 29.8) and the CRh rate was 8.8% (11 of 125 patients). The overall response rate, or ORR, among the R/R AML patients was 41.6% (52 of 125 patients), and median duration of response was 9.3 months (95% CI 5.6, 18.3) for patients who achieved a CR, 8.2 months (95% CI 5.5, 12.0) for patients who achieved a CR/CRh and 6.5 months (95% CI 4.6, 9.3) for all patients who responded. The median time to first response was 1.9 months (0.8-4.7) for all patients who responded, median time to CR was 2.8 months (0.9-8.3) for patients who achieved a CR, and median time to CR/CRh was 2.7 months (0.9-5.6) for patients who achieved a CR/CRh. At the time of the data cut-off, median OS as observed in the study had not yet been reached for patients who achieved a CR/CRh. OS was 9.3 months (95% CI 3.7, 10.8) for non-CR/CRh

responders, 3.9 months (95% CI 2.8, 5.8) for non-responders, and 8.8 months (95% CI 6.7, 10.2) overall. Of the patients who were transfusion dependent at baseline and achieved a CR, 100% became independent of platelet transfusions and 84.6% became independent of red blood cell, or RBC,

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transfusions during any 56-day post baseline period. Of the patients who were transfusion dependent at baseline and achieved a CRh, 71.4% became independent of platelet transfusions and 75.0% became independent of RBC transfusions during any 56-day post baseline period. Transfusion independence was also seen among non-CR/CRh responders and non-responders. Of the patients who were transfusion dependent at baseline and were non-CR/CRh responders, 58.3% became independent of platelet transfusions and 50% became independent of RBC transfusions during any 56-day post-baseline period. Of those who were transfusion dependent at baseline and were non-responders, 16.7% became independent of platelet transfusions and 15.4% became independent of RBC transfusions during any 56-day post-baseline period. Non-CR/CRh responders include patients with CRi, CRp and MLFS who are not CRh. An efficacy analysis was also presented for 34 untreated AML patients not eligible for standard of care therapies whose starting dose was 500 mg daily and 12 myelodysplastic syndrome, or MDS, patients in expansion cohorts whose starting dose was 500 mg daily. Data from 34 untreated AML patients demonstrated a 55.9% ORR and a CR rate of 20.6%. The median duration of response was 9.2 months (95% CI 1.9, NE), and median duration of CR has not yet been reached. Data from 12 MDS patients demonstrated a 91.7% ORR and a CR rate of 41.7%.

Phase 1b frontline combination trial

As discussed above, ivosidenib is being evaluated in a phase 1b, multicenter, international, open-label clinical trial to evaluate the safety and clinical activity of IDHIFA® or ivosidenib 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.

In December 2017, we presented interim data from this trial at ASH 2017. As of the August 1, 2017 data cut-off, in the ivosidenib arm, the most common grade 3 or higher non-hematologic AEs during the induction period were febrile neutropenia (60%), blood bilirubin increase (9%), hypertension (9%), colitis (9%), increased alanine aminotransferase (9%) and increased aspartate aminotransferase (9%). The 30 and 60-day mortality rates were both 6%, and there were no dose-limiting toxicities. The median time to ANC recovery (greater than 500/μL) was 28.5 days (95% CI 27,34). The median time to platelet recovery (greater than 50,000/μL) was 28 days (95% CI 26,34). In the ivosidenib arm the overall best response rate of combined CR and CRi/CRp was 77% (23 of 30 response-evaluable patients); among 21 patients with de novo AML, the overall best response rate of combined CR and CRi/CRp was 91% (19 of 21 patients); and among nine patients with secondary AML, the overall best response rate of combined CR and CRi/CRp was 44% (four of nine response-evaluable patients). The interim reported results from the IDHIFA® arm of this trial are discussed above under *IDHIFA® Phase 1(b) frontline combination trial*.

Phase 1/2 frontline combination trial

As discussed above, ivosidenib is being evaluated in a phase 1/2 frontline combination clinical trial, conducted by Celgene, of either IDHIFA® or ivosidenib in combination with VIDAZA® (azacitidine) in newly diagnosed AML patients not eligible for intensive chemotherapy.

In December 2017, we presented interim data from this trial at ASH 2017. As of the September 1, 2017 data cut-off, the median age of patients treated in the ivosidenib arm was 76 (all 65 years old or older), and the most common grade 3-4 hematologic AEs were anemia (18%), febrile neutropenia (18%), neutropenia (9%) and thrombocytopenia (9%), and the most common grade 3-4 non-hematologic AE was pneumonia (18%). IDH differentiation syndrome was reported in one patient. In the ivosidenib arm eight of 11 patients had a response, including four CRs, one CRi, one PR and two MLFSs.

AGILE

Ivosidenib is being evaluated in AGILE, a global, registration-enabling phase 3 clinical trial, combining ivosidenib and VIDAZA® in newly diagnosed AML patients with an IDH1 mutation who are ineligible for intensive chemotherapy. The trial has a primary endpoint of overall survival. The trial is currently open for enrollment and we expect to complete enrollment in 2021.

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Phase 3 frontline combination trial

As discussed above, we plan to support, with Celgene, the initiation of an intergroup sponsored, global, registration-enabling phase 3 trial combining ivosidenib or IDHIFA® and standard induction (7+3) and consolidation chemotherapy with a primary endpoint of event free survival in frontline AML patients with an IDH1 or IDH2 mutation in the fourth quarter of 2018.

Phase 1 clinical trial (advanced solid tumors)

Ivosidenib is being evaluated in a phase 1 multicenter, open-label, dose-escalation and expansion clinical trial, designed to assess its safety, clinical activity and tolerability as a single agent in patients with advanced solid tumors with an IDH1 mutation, including glioma, cholangiocarcinoma, and chondrosarcomas. Enrollment is now complete for 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 ivosidenib once daily.

In June 2017, we reported updated interim data from the dose escalation and dose expansion cohorts of our ongoing phase 1 clinical trial evaluating ivosidenib in patients with IDH1 mutant-positive cholangiocarcinoma at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, Illinois. As of the March 10, 2017 data cut-off, 73 patients with IDH1 mutant positive cholangiocarcinoma had been treated with single agent ivosidenib in the dose escalation (n=24) and expansion cohorts (n=49). Thirteen patients remained on treatment. Ivosidenib was administered at the following dose levels and schedules in the dose-escalation cohort: 100 mg twice daily, and 300, 400, 500, 800 and 1200 mg once a day over a 28 day cycle length. In the dose expansion cohort, patients received 500 mg once a day, which was the selected dose for the ongoing Phase 3 ClarIDHy trial, described below. Among the cholangiocarcinoma population in the trial, the median age is 60 (ranging from 32 to 81). Sixty-five patients had intrahepatic cholangiocarcinoma and eight had extrahepatic disease. The median number of prior systemic therapies was two (ranging from one to five) and 97% of patients received a prior gemcitabine-based chemotherapy regimen. A safety analysis conducted for all 73 treated patients as of the data cut-off demonstrated that ivosidenib was well-tolerated with a favorable safety profile in IDH1 mutant positive cholangiocarcinoma patients. No dose limiting toxicities or treatment-related deaths were observed. The majority of AEs reported were mild to moderate, with the most common regardless of causality being fatigue, nausea, diarrhea and decreased appetite. Four patients experienced drug-related AEs of at least grade 3: two at the 500 mg dose level, fatigue (n=1) and blood alkaline phosphatase increases (n=1), and two at the 1200 mg dose level, fatigue (n=1) and blood phosphorous decreases (n=1). One patient had a dose reduction for a grade 2 AE of worsening leg cramps that was considered to be possibly drug-related. Efficacy data from all 73 treated patients as of the data cut-off showed four patients (5%) experienced a confirmed partial response (one at 300 mg daily and three at 500 mg daily). A partial response is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters according to the Response Evaluation Criteria in Solid Tumors (RECIST v1.1). Forty-one patients (56%) experienced stable disease. Landmark analyses of progression free survival, or PFS, at six and 12 months were 38.5% and 20.7% respectively. The median PFS was 3.8 months (95% CI 3.6, 7.3). Ivosidenib treatment inhibited plasma 2HG to within levels found in healthy volunteers, and also reduced 2HG in tumor biopsies, with 2HG levels in plasma and tumor biopsies showing a positive correlation. Pathology review of on-study tumor biopsies were conducted in a patient achieving a partial response, which showed morphologic changes suggestive of cellular differentiation which is consistent with the proposed mechanism of action of ivosidenib.

In November 2017, we reported updated interim data from the dose expansion cohort of our ongoing phase 1 clinical trial evaluating ivosidenib in patients with progressive low-grade IDH1 mutant-positive glioma at the Society for

Neuro-Oncology Annual Meeting in San Francisco, California. As of the May 12, 2017 data cut off, 35 patients (11 from dose escalation, 24 from dose expansion) with non-enhancing glioma had been treated with single agent ivosidenib. Eighteen patients (51%) remained on treatment. Twenty-four patients had World Health

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Organization (WHO) classified grade 2 tumors, eight had grade 3 tumors, one had a grade 4 tumor and two were unknown. Patients received daily doses of ivosidenib ranging from 300 mg to 900 mg. Twenty-eight patients received a daily dose of 500 mg, which was selected as the expansion dose. The median age of these patients is 38 (ranging from 21 to 71). The median treatment duration was 16 months (ranging from 1.4 to 27.1 months). The median number of prior therapies was two (ranging from one to five), and the median duration of last systemic therapy was 9.6 months. Sixty-three percent of patients had previously received temozolomide and 57% percent had previously received radiotherapy. A safety analysis conducted for all 35 treated non-enhancing glioma patients as of the data cut-off demonstrated that ivosidenib was well-tolerated with a favorable safety profile in glioma patients. No dose limiting toxicities were observed. The majority of adverse events reported by investigators were mild to moderate, with the most common being headache, diarrhea, nausea and vomiting. There were 5 patients with SAEs and all were deemed unrelated to study treatment. Efficacy data from all 35 non-enhancing glioma patients as of the data cut-off showed that two patients had a minor response by investigator assessment according to the Response Assessment in Neuro-Oncology for low grade glioma (RANO-LGG) and 29 (83%) patients had stable disease. The median PFS for all non-enhancing patients was 13 months, and the median PFS for Grade 2 patients (n=24) had not been reached. For patients in the expansion arm (n=24), the average six-month tumor growth was 24% prior to treatment and 11% following treatment with ivosidenib.

ClarIDHy

Ivosidenib is being evaluated in ClarIDHy, a registration-enabling phase 3, multicenter, randomized, double-blind, placebo-controlled clinical trial of ivosidenib in previously-treated patients with nonresectable or metastatic cholangiocarcinoma with an IDH1 mutation. The trial has an overall endpoint of PFS. The trial was initiated in December 2016 and is currently enrolling patients, and we expect to complete enrollment in 2019.

AG-881: brain penetrant 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 are currently focusing our development efforts for AG-881 in glioma. We and Celgene are developing AG-881 pursuant to the AG-881 agreements, described below.

We are conducting two 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 is 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 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 receive AG-881 to further evaluate the safety, tolerability and clinical activity of the recommended phase 2 dose.

The phase 1 trial in patients with advanced IDH1 or IDH2 mutant-positive hematologic malignancies has completed its dose escalation portion, establishing proof of mechanism as measured by reductions in 2HG levels, and is now closed for enrollment. No MTD was reached. In the phase 1 trial in IDH1 or IDH2 mutant-positive advanced solid tumors, an MTD was established and enrollment is complete.

We have not yet presented any clinical data from these trials. In October 2017, we presented the first preclinical data of AG-881 in IDH mutant-positive solid and hematologic malignancies at the AACR-NCI-EORTC International

Conference on Molecular Targets and Cancer Therapeutics in Philadelphia, Pennsylvania.

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In the first half of 2018, we intend to initiate a perioperative study with ivosidenib and AG-881 in low grade glioma to further investigate their effects on brain tumor tissue. Pursuant to the AG-881 agreements, described below, Celgene has elected not to participate in this clinical trial and, as a result, we will fund the trial ourselves. Celgene will continue to co-fund the ongoing phase 1 trials of AG-881 described above.

PKR activator program

Pyruvate kinase, or PK, is the enzyme involved in the second to last reaction in glycolysis the conversion of glucose into lactic acid. This enzyme is critical for the survival of the cell and has several tissue-specific isoforms (PKR, PKL, PKM1 and PKM2). PKR is the isoform of pyruvate kinase that is present in red blood cells. Mutations in PKR cause defects in red cell glycolysis and lead to a hematological RGD known as pyruvate kinase deficiency, or PK deficiency. Glycolysis is the only pathway available for red blood cells to maintain the production of ATP, or Adenosine-5 -triphosphate, which transports chemical energy within cells for metabolism. Accordingly, total absence of the PKR gene is not compatible with life. PK deficiency leads to a shortened life span for red blood cells and is the most common form of non-spherocytic hemolytic anemia in humans.

PK deficiency is a rare genetic disorder and disease understanding is still evolving. We estimate that the prevalence of PK deficiency is between approximately 1-in-75,000 and 1-in-200,000 people, and we believe that the disease is likely under-diagnosed. There is no unique ethnic or geographic representation of the disease. The disease manifests by mild to severe forms of anemia caused by the excessive premature destruction of red blood cells. The precise mechanism for the destruction is not well understood but is thought to result from membrane instability secondary to the metabolic defect caused by the low level of PKR enzyme. The hemolysis is extra-vascular in that the red blood cells are destroyed in small capillaries or organs and do not spontaneously break open in the circulation. PK deficiency is an autosomal recessive disease whereby all patients inherit two mutations, one from each parent. Children with the disease produce PKR enzyme that has only a fraction of the normal level of activity (generally <50%). Parents of affected children have only one copy of the mutated PKR enzyme and are clinically normal. More than 250 different mutations have been identified to date. As a result, there are many different possible mutant combinations and no one clear mutational profile. 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 in the red blood cells. A non-missense mutation is any mutation other than a missense mutation, generally resulting in little functional protein in the red blood cells. It is estimated that 58 percent of patients with PK deficiency have two missense mutations, 27 percent have one missense and one non-missense mutation, and 15 percent have two non-missense mutations. 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 genetic information. We intend to initiate a global registry for adult and pediatric patients with PK deficiency in the first quarter of 2018 to increase understanding of the long-term disease burden of this chronic anemia.

AG-348: 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. We have shown that AG-348 can restore adenosine triphosphate, or ATP, levels and decrease 2,3-diphosphoglycerate, or 2,3-DPG, levels in blood sampled from patients with PK deficiency when treated ex-vivo with AG-348. 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, and provides for potential expansion opportunities into other anemias. The FDA granted us orphan drug designation for AG-348 for treatment of patients with PK deficiency. We intend to initiate two global, pivotal trials of AG-348 in PK deficiency in the first half of 2018: ACTIVATE-T, a single arm trial of

approximately 20 regularly transfused patients, is expected to initiate in the first quarter of 2018, and ACTIVATE, a 1:1 randomized, placebo-controlled trial of approximately 80 patients who do not receive regular transfusions, is expected to initiate in the second quarter of 2018. We also expect to initiate a phase 2 proof of concept trial of AG-348 in thalassemia in the fourth quarter of 2018.

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DRIVE-PK

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 up to 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 24-week treatment period with the opportunity for continued treatment beyond 24 weeks based on safety and clinical activity.

In June 2016, we reported the first clinical data from DRIVE PK at EHA, establishing proof of concept for AG-348 as a novel, first-in-class, oral activator of both wild-type and mutated PKR enzymes.

The trial reached target enrollment of 52 patients in November 2016, and in December 2017, we reported updated data from the trial at ASH 2017. As of the July 14, 2017 data cut-off, 43 patients completed the six-month core dosing period and nine patients discontinued treatment during the core dosing period. Thirty-six of 43 patients who completed the six-month core treatment period entered the extension period. As of the data cut-off, 29 patients remained on treatment in the extension period. A safety analysis was conducted based on all 52 treated patients as of the data cut-off. AG-348 remained well-tolerated, and the majority of treatment-related AEs were Grade 1-2; the most frequent being headache, insomnia and nausea. Four patients experienced treatment-related AEs leading to discontinuation: pleural effusion (n=1), hypertriglyceridemia (n=1), pharyngitis/nausea (n=1) and anemia (n=1). Four patients experienced treatment-related SAEs: withdrawal hemolysis followed by anemia (n=1), anemia (n=1), osteoporosis (n=1) and hypertriglyceridemia (n=1). Measurements of hormone levels in men at doses less than or equal to 50 mg twice daily suggest mild aromatase inhibition by AG-348, and ongoing follow-up will continue to assess the potential clinical significance of this aromatase inhibition. Twenty-six of 52 patients (50%) overall and 25 of 42 patients (60%) with at least one missense mutation achieved rapid and sustained Hb increases from baseline of greater than 1.0 g/dL as of the data cut-off. In patients who had Hb increases of greater than 1.0 g/dL, the mean maximum Hb increase was 3.4 g/dL (range 1.1 to 5.8 g/dL). The median time to first Hb increase of greater than 1.0 g/dL was 10 days (range 7 to 187 days). The median baseline Hb in patients who experienced a maximum Hb increase of greater than 1.0 g/dL was 9.7 g/dL (range 7.3 to 12.3 g/dL) compared to 8.0 g/dL (range 6.5 to 10.1 g/dL) in patients who did not experience the increase.

ACTIVATE/ACTIVATE-T

We intend to initiate two global, pivotal trials of AG-348 in PK deficiency in the first half of 2018: ACTIVATE-T, a single arm trial of approximately 20 regularly transfused patients, is expected to initiate in the first quarter of 2018, and ACTIVATE, a 1:1 randomized, placebo-controlled trial of 80 patients who do not receive regular transfusions, is expected to initiate in the second quarter of 2018. The primary endpoint of the ACTIVATE trial is the proportion of patients who achieve at least a 1.5 g/dL increase in Hb sustained over multiple visits, and the primary endpoint of the ACTIVATE-T trial is a reduction in transfusion burden over a six-month period compared to the patient s transfusion history.

In addition to the above planned and ongoing clinical trials of AG-348, we plan to initiate a phase 2 proof of concept trial of AG-348 in thalassemia in the fourth quarter of 2018.

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

Targeting Mat2A for the treatment of MTAP-deleted cancers

AG-270, a MAT2A inhibitor, is our development candidate focused on MTAP-deleted cancers. We submitted an IND for AG-270 in November 2017 and, in December 2017, the FDA concluded that we may proceed with a proposed phase 1 dose-escalation trial in multiple tumor types carrying an MTAP deletion, which we expect to initiate in the first quarter of 2018.

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MTAP is a metabolic gene that is deleted in approximately 15 percent of all cancers. We have shown in preclinical studies that MTAP deletion predicts sensitivity to inhibition of a subset of enzymes involved in the synthesis or utilization of the methyl donor S-adenosylmethionine, or SAM. Among this subset of enzymes, we believe that MAT2A is principally responsible for the synthesis of SAM. We have discovered small molecule inhibitors of MAT2A, including AG-270, that reduce SAM production and cause MTAP-null antiproliferative effects in cancer cell lines in vitro and in MTAP-deleted tumor models in vivo. MTAP deletion is readily detected by a genomic or immunohistochemistry test, thus allowing the selection of patients predicted to be sensitive to the therapy.

In March 2017, we announced that Celgene designated AG-270 as a development candidate under our 2016 research collaboration agreement with Celgene, or the 2016 agreement. Pursuant to the 2016 agreement, Celgene paid us an $8.0 million designation fee upon its designation of AG-270 as a development candidate. Exploratory research, drug discovery and early development of AG-270 is led by us, and Celgene will have an opt-in right on AG-270 up through phase 1 dose escalation for at least a $30.0 million fee. Upon opt-in, we and Celgene will have global co-development and co-commercialization rights with a worldwide 50/50 cost and profit share on AG-270, and we will be eligible for up to $168.8 million in clinical and regulatory milestone payments.

Targeting DHODH for the treatment of hematologic malignancies

In January 2018, we announced that we plan to submit an IND for our latest development candidate, an inhibitor of DHODH, licensed by us from Aurigene Discovery Technologies Limited, for the treatment of hematologic malignancies in the fourth quarter of 2018. We have discovered a lineage-specific dependence on DHODH in hematologic malignancies, particularly AML and diffuse large B-cell lymphoma. DHODH catalyzes a critical step in the biosynthesis of RNA and DNA. We believe that DHODH inhibition will be differentiated from standard-of-care therapies, both by exhibiting activity in cancers that are resistant to standard-of-care chemotherapeutics and through a mechanism of anti-tumor effect that combines cell growth arrest and cellular differentiation.

Collaborations with Celgene

2016 agreement

In May 2016, we entered into the 2016 agreement focused on MIO, a developing field which aims to modulate the activity of relevant immune cells by targeting critical metabolic nodes, thereby, enhancing the immune mediated anti-tumor response. We are leveraging our proprietary metabolic, target discovery and validation platforms with the goal of unlocking promising targets in this field. The immune system s ability to attack tumors is highly regulated by cellular metabolism. We believe that the emerging field of MIO has great potential to provide novel insights and targets for cancer immunotherapy in solid and hematologic malignancies.

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.

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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 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, low 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.

As described above, in March 2017, we announced that Celgene designated the development candidate focused on MTAP-deleted cancers as a development candidate under the 2016 agreement.

Ivosidenib letter agreement

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 ivosidenib 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 ivosidenib and the IDH1 program. Neither party will have any financial obligation, including royalties or milestone payments, to the other concerning ivosidenib 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 ivosidenib 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.

AG-881 agreements

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

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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.

2010 agreement

In April 2010, we entered into the 2010 agreement focused on cancer metabolism. The 2010 agreement was amended in October 2011 and July 2014. The goal of the collaboration was to discover, develop and commercialize disease-altering therapies in oncology based on the Company s cancer metabolism research platform. We initially led discovery, preclinical and early clinical development for all cancer metabolism programs under the collaboration. The discovery phase of the collaboration under the 2010 agreement expired in April 2016.

We nominated IDHIFA® and ivosidenib 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 IDHIFA®. In addition to contributing our scientific and translational expertise, we continued to conduct certain clinical development and regulatory activities within the IDHIFA® 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 ivosidenib outside the United States. Following Celgene s exercise of this option, we retained development and commercialization rights for ivosidenib in the United States. Pursuant to the ivosidenib letter agreement, we terminated the 2010 agreement, effective as of August 15, 2016, as to the program directed to the IDH1 target, for which ivosidenib is the lead development candidate. Consequently, the sole program remaining under the 2010 agreement is IDHIFA®, a co-commercialized licensed program. Under the terms of the 2010 agreement, Celgene funds global development and commercialization of IDHIFA®. We have exercised our right to participate in a portion of commercialization activities in the United States for IDHIFA® in accordance with the applicable commercialization plan. The development and commercialization of IDHIFA® is managed by a set of joint committees comprised of equal numbers of representatives from each party. The joint steering committee oversees and coordinates the overall conduct of the collaboration. The joint development committee oversees and coordinates development (including manufacturing of clinical supply) of IDHIFA®. The joint commercialization committee will oversee the commercialization (including manufacturing of commercial supply) of the program.

Under the 2010 agreement, we are eligible to receive up to $120 million in potential milestone payments payable for the IDHIFA® program, as well as royalties at tiered, low- to mid-teen percentage rates on net sales, and we have the option to participate in the development and commercialization of certain products in the United States. In the first quarter of 2016, we received a $25 million milestone payment under the 2010 agreement in connection with the initiation of the IDHENTIFY clinical trial.

Risks associated with our business

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

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability. As of September 30, 2017, we had an accumulated deficit of

$709.8 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.

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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.

IDHIFA®, or any of our product candidates that receive marketing approval in the future, may fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community, and our and our collaborator s commercialization efforts may not be successful.

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

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 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 in the United States for IDHIFA®, ivosidenib, AG-881 and AG-348 as compositions of matter; we do not own or license issued patents for all of our lead product candidates in other jurisdictions. 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.

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	7,089,553 shares
Common stock to be outstanding after this offering	55,707,542 shares
Option to purchase additional shares	The underwriters have an option for a period of 30 days to purchase up to 1,063,433 additional shares of our common stock.
Use of proceeds	We intend to use the net proceeds from this offering to fund our ongoing research and clinical development efforts, including preparation for the anticipated regulatory approval and commercial launch of ivosidenib; ongoing enrollment in our phase 3 ClarIDHy and AGILE trials with ivosidenib; initiation and enrollment in a planned intergroup sponsored phase 3 trial combining ivosidenib and standard induction and consolidation chemotherapy in frontline AML patients; initiation and enrollment in our planned pivotal trials of AG-348 in PK deficiency, ACTIVATE and ACTIVATE-T, our planned phase 2 trial of AG-348 in thalassemia, our planned phase 1 study of AG-270 in MTAP-deleted cancers, and our planned perioperative study with ivosidenib and AG-881 in IDH1 mutant-positive low-grade glioma; IND-enabling activities and, if successful, a phase 1 clinical trial for our DHODH inhibitor; the advancement of our late-stage preclinical pipeline; our other ongoing and planned clinical trials; and working capital and other general corporate purposes. See Use of proceeds for more information.
Risk factors	See Risk factors beginning on page S-21 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 48,617,989 shares of our common stock outstanding as of September 30, 2017.

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

- 5,820,611 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2017 at a weighted-average exercise price of $48.68 per share;

120,000 shares of common stock issuable upon vesting of restricted stock units outstanding as of September 30, 2017;

191,374 shares of common stock issuable upon vesting of performance-based stock units outstanding as of September 30, 2017;

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1,275,813 shares of common stock reserved as of September 30, 2017 for future issuance under our equity incentive plans; and

213,791 shares of common stock reserved as of September 30, 2017 for future issuance under our 2013 employee stock purchase plan.

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

no exercise of the outstanding options described above; and

no exercise by the underwriters of their option to purchase additional shares.

Celgene Corporation, or Celgene, an existing stockholder and our strategic alliance partner in the fields of cancer metabolism and metabolic immuno-oncology, has indicated an interest in purchasing an aggregate of 851,154 shares of our common stock in this offering at the public offering price. However, because an indication of interest is not a binding agreement or commitment to purchase, Celgene may determine to purchase fewer shares than it has indicated an interest in purchasing or not to purchase any shares in this offering. In addition, the underwriters could determine to sell fewer shares to Celgene than Celgene indicated an interest in purchasing or not to sell any shares to Celgene. The underwriters will receive the same underwriting discount on any shares purchased by Celgene as they will on any other shares sold to the public in this offering. Any shares sold to Celgene will be subject to the lock-up agreement described under Underwriting.

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Summary consolidated financial data

The following table summarizes our consolidated financial data. We have derived the following summary of our consolidated statement of operations data for the nine months ended September 30, 2017 and the consolidated balance sheet data as of September 30, 2017 from our unaudited condensed consolidated financial statements incorporated by reference in this prospectus supplement from our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2017. We derived the consolidated statement of operations data for the years ended December 31, 2016, 2015 and 2014 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, 2016. 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, 2016 and our unaudited Quarterly Report on Form 10-Q for the nine months ended September 30, 2017 and incorporated by reference in this prospectus supplement. For more details on how you can obtain the documents incorporated by reference in this prospectus supplement, see Where you can find more information and Incorporation of documents by reference appearing elsewhere in this prospectus supplement. Our historical results are not necessarily indicative of future results.

(in thousands, except share and per share amounts)	Nine months ended September 30, 2017	Year Ended December 31, 2016	2015	2014
Consolidated statements of operations:				
Collaboration revenue related party	$ 32,497	$ 69,892	$ 59,119	$ 65,358
Royalty revenue related party	715			
Total revenue	33,212	69,892	59,119	65,358
Operating expenses:				
Research and development (net of $6,343, $19,714 and $25,173 of cost reimbursement from related party for the nine months ended September 30, 2017 and the years ended December 31, 2016 and 2015, respectively)	215,465	220,163	141,827	100,371
General and administrative	48,411	50,714	35,992	19,120
Total operating expenses	263,876	270,877	177,819	119, 491
Loss from operations	(230,664)	(200,985)	(118,700)	(54,133)
Interest income	4,279	2,514	968	203
Loss before income taxes	(226,385)	(198,471)	(117,732)	(53,930)
(Benefit) provision for income taxes				(426)
Net loss	(226,385)	(198,471)	(117,732)	(53,504)
Net loss per share basic and diluted	$ (4.94)	$ (5.07)	$ (3.15)	$ (1.59)
Weighted-average number of common shares used in net loss per share basic and diluted	45,851,203	39,126,400	37,429,262	33,667,024

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(in thousands)	As of September 30, 2017 Actual	As Adjusted(1)
Condensed consolidated balance sheet data:		
Cash, cash equivalents and marketable securities	$ 641,732	$ 1,090,232
Total assets	687,200	1,135,700
Total liabilities	237,394	237,394
Common stock	49	56
Additional paid-in capital	1,160,048	1,608,541
Accumulated deficit	(709,776)	(709,776)
Total stockholders equity	449,806	898,306

(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 $67.00 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, 2016 and our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2017, 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 $50.87 per share, after giving effect to the sale by us of shares in this offering at the public offering price of $67.00 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.

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

We expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity

securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to those of holders of our common stock.

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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.

Sales of substantial amounts of our common stock in the public markets, or the perception that such sale might occur, could reduce the price that our common stock might otherwise attain.

Sales of a substantial amount of shares of our common stock in the public market, particularly sales by our directors, executive officers and significant stockholders, or the perception that these sales could occur, could cause the market price of our common stock to decline and may make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

Our executive officers and directors have entered into lock-up agreements with the underwriters under which they have agreed, subject to specific exceptions described under Underwriting, not to sell, directly or indirectly, any shares of common stock without the permission of J.P. Morgan Securities LLC and Goldman Sachs & Co. LLC for a period of 45 days following the date of this prospectus. Similarly, we and Celgene have also agreed, subject to specific exceptions described under Underwriting, not to sell, directly or indirectly, any shares of common stock without the permission of J.P. Morgan Securities LLC and Goldman Sachs & Co. LLC for a period of 60 days following the date of this prospectus. We refer to such periods as the lock-up periods. When the lock-up periods expire, we and the shareholders who are subject to a lock-up agreement will be able to sell shares in the public market. Sales of a substantial number of such shares upon expiration of the lock-up agreements, the perception that such sales may occur, or early release of these agreements, could cause our market price to fall or make it more difficult for you to sell your common stock at a time and price that you deem appropriate.

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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, MAT2A and DHODH as therapeutic targets;
- the potential benefits of our product candidates targeting IDH1, IDH2 or pyruvate kinase-R mutations MAT2A or DHODH, including ivosidenib, IDHIFA® (ensasidenib), AG-881, AG-348 and AG-270;
- our plans to develop and commercialize our product candidates, including our ability to successfully commercialize IDHIFA® with our partner Celgene Corporation, or Celgene, and to obtain regulatory approval for, and successfully commercialize, ivosidenib;
- our plans to develop and commercialize our product candidates;
- our collaborations with Celgene and related subsidiaries;
- 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 7,089,553 shares of our common stock in this offering will be approximately $448.5 million after deducting 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 $515.8 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to fund our ongoing research and clinical development efforts, including preparation for the anticipated regulatory approval and commercial launch of ivosidenib; ongoing enrollment in our phase 3 ClarIDHy and AGILE trials with ivosidenib; initiation and enrollment in a planned intergroup sponsored phase 3 trial combining ivosidenib and standard induction and consolidation chemotherapy in frontline AML patients; initiation and enrollment in our planned pivotal trials of AG-348 in PK deficiency, ACTIVATE and ACTIVATE-T, our planned phase 2 trial of AG-348 in thalassemia, our planned phase 1 study of AG-270 in MTAP-deleted cancers, and our planned perioperative study with ivosidenib and AG-881 in IDH1 mutant-positive low-grade glioma; IND-enabling activities and, if successful, a phase 1 clinical trial for our DHODH inhibitor; the advancement of our late-stage preclinical pipeline; our other ongoing and planned clinical trials; and working capital and other general corporate purposes.

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

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

Pending use of the proceeds as described above, we intend to invest the proceeds in a variety of capital preservation investments, including short-term, interest-bearing, investment-grade instruments, 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
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	$ 54.99	$ 35.84
Fourth quarter	$ 67.74	$ 40.59
2017		
First quarter	$ 58.65	$ 39.24
Second quarter	$ 59.58	$ 45.11
Third quarter	$ 67.62	$ 50.91
Fourth quarter	$ 72.73	$ 51.62
2018		
First quarter (through January 18, 2018)	$ 76.02	$ 56.50

On January 18, 2018, the last reported sale price of our common stock as reported on The Nasdaq Global Select Market was $68.15 per share, and we had approximately 15 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend policy

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

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Capitalization

The following table sets forth our consolidated cash, cash equivalents and marketable securities and capitalization as of September 30, 2017, as follows:

- on an actual basis; and
- on an as adjusted basis to give effect to our issuance and sale of 7,089,553 shares of our common stock in this offering at the public offering price of $67.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the following table together with Description of capital stock appearing in the accompanying prospectus, and our consolidated financial statements and related notes to those statements and the Management s Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the year ended December 31, 2016, which is incorporated by reference in this prospectus supplement.

	As of September 30, 2017	
(in thousands, except share and per share data)	**Actual**	**As Adjusted**
Cash, cash equivalents and marketable securities	$ 641,732	$ 1,090,232
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, 48,617,989 shares issued and outstanding, actual; 55,707,542 shares issued and outstanding, as adjusted	$ 49	$ 56
Additional paid-in capital	$ 1,160,048	$ 1,608,541
Accumulated other comprehensive loss	$ (515)	$ (515)
Accumulated deficit	$ (709,776)	$ (709,776)
Total stockholders equity	$ 449,806	$ 898,306
Total capitalization	$ 449,806	$ 898,306

The table above does not include:

- 5,820,611 shares of common stock issuable upon exercise of stock options outstanding as of September 30, 2017 at a weighted-average exercise price of $48.68 per share;

120,000 shares of common stock issuable upon vesting of restricted stock units outstanding as of September 30, 2017;

191,374 shares of common stock issuable upon vesting of performance-based stock units outstanding as of September 30, 2017;

1,275,813 shares of common stock reserved as of September 30, 2017 for future issuance under our equity incentive plans; and

213,791 shares of common stock reserved as of September 30, 2017 for future issuance under our 2013 employee stock purchase plan.

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Dilution

As of September 30, 2017, our net tangible book value was approximately $449.8 million, or approximately $9.25 per share. Net tangible book value per share represents the amount of our total tangible assets less total liabilities divided by the 48,617,989 shares of our common stock outstanding as of September 30, 2017. After giving effect to our sale of the shares of common stock in this offering, after deducting underwriting discounts and commissions and estimated offering expenses, the net tangible book value as of September 30, 2017 would have been approximately $898.3 million, or approximately $16.13 per share. This represents an immediate increase in net tangible book value of $6.88 per share to existing stockholders and an immediate dilution in net tangible book value of $50.87 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		$ 67.00
Net tangible book value per share as of September 30, 2017	$ 9.25	
Increase in net tangible book value per share attributable to new investors	$ 6.88	
Net tangible book value per share as of September 30, 2017 after giving effect to this offering		$ 16.13
Dilution in net tangible book value per share to new investors		$ 50.87

As of September 30, 2017, there were:

- 5,820,611 shares of common stock issuable upon exercise of stock options outstanding at a weighted-average exercise price of $48.68 per share;
- 120,000 shares of common stock issuable upon vesting of restricted stock units outstanding;
- 191,374 shares of common stock issuable upon vesting of performance-based stock units outstanding;
- 1,275,813 shares of common stock reserved for future issuance under our equity incentive plans; and
- 213,791 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

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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.

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.

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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 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 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.

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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.

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, Goldman Sachs & Co. LLC and Cowen and Company, LLC are acting 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	2,623,135
Goldman Sachs & Co. LLC	2,552,239
Cowen and Company, LLC	1,347,015
RBC Capital Markets, LLC	283,582
SunTrust Robinson Humphrey, Inc.	283,582
Total	7,089,553

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 $2.211 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 1,063,433 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 $3.685 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	$ 67.000	$ 475,000,051	$ 546,250,062
Underwriting discounts and commissions to be paid by us	$ 3.685	$ 26,125,003	$ 30,043,753
Proceeds, before expenses, to us	$ 63.315	$ 448,875,048	$ 516,206,309

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 $375,000. We have agreed to reimburse the underwriters $30,000 for expenses related to any filing with, and the clearance of this offering by, the Financial Industry Regulatory Authority, Inc.

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

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. LLC for a period of 60 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 60-day restricted period described above shall enter into an agreement substantially in the form described thereby.

Our directors, executive officers and Celgene Corporation 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 45 days, with respect to our directors and executive officers and 60 days, with respect to Celgene Corporation, after the date of this prospectus supplement, may not, without the prior written consent of J.P. Morgan Securities LLC and Goldman Sachs & Co. LLC, (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, officers and shareholder 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, officer, shareholder or the immediate family of such person in a transaction not involving a disposition for value, (C) transfers or dispositions of shares of our common stock or other securities to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of

which are held by the director, officer, shareholder or the immediate family of such person in a transaction not involving a disposition for value, (D) transfers or dispositions of shares of our common stock

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or other securities by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the director, officer, or shareholder (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. LLC 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, officer or shareholder may (i) transfer such person s shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock to us pursuant to any contractual arrangement in effect on the date of the lock-up agreement that provides for the repurchase of such person s common stock or such other securities by us or in connection with such person s termination of employment with us, provided that no filing by any party under the Exchange Act or other public announcement may be required or voluntarily made in connection with such transfer, disposition or distribution 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, officer or shareholder or any other person in connection therewith, in each case during the restricted period or any extension thereof pursuant to the lock-up agreement, (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, officer or shareholder, may be required or voluntarily made in connection with such transfer, other than a filing on a Form 5 made after the expiration of the restricted period referred to above 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 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.

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Selling restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required.

The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

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 (NI 33-105), 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.

Prohibition of sales to EEA retail investors

The securities are not intended to be offered, sold or otherwise made available to and should not be offered, sold or otherwise made available to any retail investor in the European Economic Area (EEA). For these purposes, a retail investor means a person who is one (or more) of: (i) a retail client as defined in point (11) of Article 4(1) of Directive 2014/65/EU (as amended, MiFID II); or (ii) a customer within the meaning of Directive 2002/92/EC

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(as amended, the Insurance Mediation Directive), where that customer would not qualify as a professional client as defined in point (10) of Article 4(1) of MiFID II; or (iii) not a qualified investor as defined in Directive 2003/71/EC (as amended, the Prospectus Directive). Consequently no key information document required by Regulation (EU) No 1286/2014 (as amended, the PRIIPs Regulation) for offering or selling the securities or otherwise making them available to retail investors in the EEA has been prepared and therefore offering or selling the securities or otherwise making them available to any retail investor in the EEA may be unlawful under the PRIIPS Regulation.

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,

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

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Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

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

Japan

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

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Legal matters

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

Experts

The consolidated financial statements of Agios Pharmaceuticals, Inc. appearing in Agios Pharmaceuticals, Inc. s Annual Report (Form 10-K) for the year ended December 31, 2016, and the effectiveness of Agios Pharmaceuticals, Inc. s internal control over financial reporting as of December 31, 2016, 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 by reference herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements and the effectiveness of Agios Pharmaceuticals, Inc. s internal control over financial reporting as of the respective dates (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as an expert 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, 2016;

Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017, June 30, 2017 and September 30, 2017;

The information included in our definitive proxy statement on Schedule 14A, filed with the SEC on April 24, 2017, to the extent specifically incorporated by reference into Part III of the Annual Report on Form 10-K for the fiscal year ended December 31, 2016;

Our Current Reports on Form 8-K dated January 4, 2017, January 9, 2017, March 13, 2017, April 19, 2017, May 5, 2017, May 31, 2017, June 6, 2017, June 14, 2017, June 26, 2017, August 1, 2017, November 17, 2017, November 22, 2017, December 5, 2017, December 11, 2017, December 19, 2017, and January 8, 2018; 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 or incorporated by reference 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 8, 2017

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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 3 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, 2016, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2017 Annual Meeting of Stockholders;

- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017, June 30, 2017 and September 30, 2017;

- Current Reports on Form 8-K filed January 4, 2017, January 9, 2017, March 13, 2017, April 19, 2017, May 5, 2017, May 31, 2017, June 6, 2017, June 14, 2017, June 26, 2017, August 1, 2017, November 17, November 22, 2017 and December 5, 2017; 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:

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CAUTIONARY NOTE REGARDING 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 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 current and future preclinical studies and clinical trials, and our research and development programs;
- the potential of IDH1/IDH2 and pyruvate kinase-R mutations and the methylithioadenosine phosphorylase, or MTAP , pathway as therapeutic targets;
- the potential benefits of our product candidates targeting IDH1/IDH2 or pyruvate kinase-R mutations or the MTAP pathway, including ivosidenib, IDHIFA® (ensasidenib), AG-881, AG-348 and AG-270;
- our plans to develop and commercialize our product candidates, including our ability to successfully commercialize IDHIFA® with our partner Celgene Corporation;
- our collaborations with Celgene Corporation and related subsidiaries;
- 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; 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 the fundamental transformation of patients lives through scientific leadership in the field of cellular metabolism, with the goal of making transformative, first- or best-in-class medicines. Our areas of focus are: cancer metabolism; rare genetic diseases, which are diseases that are directly caused by changes in genes or chromosomes, often passed from one generation to the next; and metabolic immuno-oncology, which is a developing field that aims to modulate the activity of relevant immune cells (or tumor microenvironment) by targeting critical metabolic nodes, thereby enhancing the immune mediated anti-tumor response. In each of these areas, we are seeking to unlock the biology of cellular metabolism as a platform to create transformative therapies.

We were incorporated under the laws of the State of Delaware in August 2007. Our principal 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 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,				
	2017	2016	2015	2014	2013	2012
Consolidated ratios of earnings to fixed charges(1)(2)	N/A	N/A	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	N/A	N/A

1) Due to our losses for the nine months ended September 30, 2017 and for the years ended December 31, 2016, 2015, 2014, 2013, and 2012, the coverage ratio was less than 1:1.
2) We would have needed to generate additional earnings of $230.7 million, $201.0 million, $118.7 million, $54.6 million, $38.3 million, and $25.8 million for the nine months ended September 30, 2017 and for the years ended December 31, 2016, 2015, 2014, 2013, and 2012, respectively, to cover our fixed charges in those periods.
3) We would have needed to generate additional earnings of $230.7 million, $201.0 million, $118.7 million, $54.6 million, $42.5 million, and $33.2 million for the nine months ended September 30, 2017 and for the years ended December 31, 2016, 2015, 2014, 2013, and 2012, 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. The senior indenture and the subordinated indenture are referred to individually as an indenture and together as the indentures and the senior trustee and the subordinated trustee are referred to individually as a trustee and together as the trustees. This section summarizes some of the provisions of the indentures and is qualified in its entirety by the specific text of the indentures, including definitions of terms used in the indentures. Wherever we refer to particular sections of, or defined terms in, 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.

Neither indenture 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 equally in right of payment 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 any subordinated debt securities the terms on which they are subordinated;

the initial aggregate principal amount of the debt securities;

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

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, 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 method of determination of such 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 the debt securities will be subject to the defeasance provisions 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;

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

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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 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 with respect to a particular series of senior debt securities, 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 with respect to a particular series of senior debt securities, 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;
- 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
- we have delivered to the senior trustee an officer s certificate and an opinion of counsel, each stating that the consolidation, merger, conveyance, transfer or lease and, if a supplemental indenture is required in connection with such transaction, such supplemental indenture, comply with the senior indenture and all conditions precedent provided for in the senior indenture relating to such transaction have been complied with.

The restrictions described in the bullets above do not apply (1) to our consolidation with or merging into one of our affiliates, if our board of directors determines in good faith that the purpose of the consolidation or merger is principally to change our state of incorporation or our form of organization to another form or (2) if we merge with or into a single direct or indirect wholly-owned subsidiary of ours.

The surviving business entity will succeed to, and be substituted for, us under the senior indenture and the senior debt securities and, except in the case of a lease, we shall be released from all obligations under the senior indenture and the senior debt securities.

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).

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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 with respect to senior debt securities of each series:

- 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.

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 automatically 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 a continuing 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 (other than any such default in payment resulting solely from an acceleration of the 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.

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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.

These limitations, however, do not apply to the right of any holder of a senior debt security of any affected series 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 have paid or caused to be paid the principal of and interest on all senior debt securities of such series (with certain limited exceptions) when due and payable; or
- we deliver to the senior trustee for cancellation all senior debt securities of such series theretofore authenticated under the senior indenture (with certain limited exceptions); 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 under arrangements satisfactory to the senior trustee) and we deposit in trust an amount of cash or a combination of cash and U.S. government or U.S. government agency obligations (or in the case of senior debt securities denominated in a foreign currency, foreign government securities or foreign government agency securities) sufficient to make interest, principal and any other payments on the debt securities of that series on their various due dates.

and if, in any such case, we also pay or cause to be paid all other sums payable under the senior indenture, as and when the same shall be due and payable and we deliver to the senior trustee an officer s certificate and an opinion of counsel, each stating that these conditions have been satisfied.

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

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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 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 cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign 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.

Covenant Defeasance. Without any change in 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 cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign 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.

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Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities of any series 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, or the Trust Indenture Act ;

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, change or eliminate any of the provisions of the senior indenture in respect of one or more series of senior debt securities, provided that any such addition, change or elimination shall (a) neither (1) apply to any senior debt security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (2) modify the rights of the holder of any such senior debt security with respect to such provision or (b) become effective only when there is no senior debt security described in clause (a)(1) outstanding;

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.

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 each series affected by the amendment or modification (voting as a separate series); 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 for 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;

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waives a continuing default in the payment of principal of or interest on the senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities);

changes the provisions relating to the waiver of past defaults 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;

adversely affects the right to convert or exchange senior debt securities into common stock or other property in accordance with the terms of the senior debt securities; 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 incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or any of our 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 amounts 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.

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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

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 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 incorporated by reference into 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.

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 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.

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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

- 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;

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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 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 Corporation 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.

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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.

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.

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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.

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

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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 two business days, unless the parties to any such trade expressly agree otherwise or the securities are sold by us to an underwriter in a firm commitment underwritten offering. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two 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 second 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 in more than two 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 (Form 10-K) for the year ended December 31, 2016, and the effectiveness of Agios Pharmaceuticals, Inc. s internal control over financial reporting as of December 31, 2016, 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 in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements and the effectiveness of Agios Pharmaceuticals, Inc. s internal control over financial reporting as of the respective dates (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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