Agios Pharmaceuticals

Equity Research

Company Quick Take

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Price: $47.50 (06/13/2014)
Price Target: NA

OUTPERFORM (1)

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Key Data

Symbol	NASDAQ: AGIO
Market Cap (MM)	$1,612.9

AG-221 Continues To Impress

The Cowen Insight

Yesterday, Agios reported updated Ph I data on AG-221 for r/r AML. AG-221 continues to induce impressive single-agent responses that are increasingly durable, while maintaining its benign safety profile. Though early in development, we believe AG-221 will become a standard treatment option for IDH2-mutant AML patients. We expect newsflow from AGIO's 3 clinical assets to drive stock outperformance.

Impressive Single-Agent Activity Looking Increasingly Durable. On Saturday, at the EHA meeting, Agios presented updated data from its Phase I single-agent, dose escalation trial on AG-221 in IDH2-mutant hematologic malignancies, including patients with relapsed/refractory AML and MDS. At the data cutoff of May 23, 2014, 35 patients had been treated in six dose cohorts (30 mg BID, 50 mg BID, 75 mg BID, 100 mg QD, 100 mg BID, and 150 mg QD). There were 25 evaluable patients (21 r/r AML, 4 MDS), of which 14 patients achieved objective responses (6 CR, 2 CRp, 1 CRi, and 5 PR). Of the 14 responding patients, 12 patients remain on study (one went on to bone marrow transplantation and one died from a surgical complication), suggesting some durability in response. None of the 12 patients have progressed on treatment after 1-4 months on AG-221. Consultants have previously suggested that even the ~2 month max duration of response observed at AACR was impressive. Hence we believe AG-221 is now in good stead in terms of durability of effect. As patient numbers are still small and responses have been observed across all dose cohorts, it is too early to have a view on whether higher doses are associated with more or deeper responses. However, Agios believes there is some suggestion that higher doses are inducing responses more quickly. In addition to the 14 responses, 5 patients have experienced stable disease and are continuing treatment, and 7 patients progressed and died. Of the 10 non-evaluable patients, 7 have died and 3 were treated too recently to have been evaluated. Agios is hopeful that with greater follow up some stable disease patients and inevaluable patients might convert to responders.

Critics will likely point out that the response rates reported at EHA are directionally lower than those observed at AACR in April. For example, looking at the evaluable patient numbers, the ORR was 86% at AACR vs. 56% at EHA. The response rate inclusive of all treated patients was 60% at AACR and 40% at EHA. This variability may in part be explained by the fact that these "point in time" analyses require an essentially random cut off date, and do not permit all patients the opportunity to reach a response. Regardless of the variability in response rate between the EHA and AACR updates, we remind investors that our consultants had previously indicated that a 25% response rate would be impressive for any new single agent in r/r AML, and the AG-221 data clearly exceed that bar. Moreover, the incremental data on durability of response increases our confidence that AG-221 will become a leading drug for IDH2 mutant r/r AML, and possibly also for IDH2 mutant MDS (though the numbers are small).

Safety Profile Looks Clean; Expansion Cohorts To Start H2:14. AG-221 was well tolerated and continues to demonstrate a very favorable safety profile relative to alternative agents for AML. Higher dose cohorts have yet to uncover any clear drug related AEs or potential dose limiting toxicity. The most common AEs were Grade 1/2 and included nausea, pyrexia, and thrombocytopenia. Four patients experienced potential drug related severe AEs including confusion, respiratory failure, leukocytosis, anorexia, nausea, and diarrhea.

Agios will proceed with dose escalation in hopes of identifying an optimal dose for further study. The company is committed to identifying a suitable dose in the coming months, and initiating a four Phase II expansion cohorts of 25 patients each. These will include (1) r/r AML patients (>60 years), (2) r/r AML patients (<60 years), (3) newly diagnosed AML patients, who decline standard of care chemotherapy, and (4) patients with other IDH2 mutant hematologic malignancies (likely MDS, angioimmunoblastic T-cell Lymphoma (AITL), and myeloma). The company expects to initiate these expansion cohorts in H2:14.

What's Next For Agios? Initiate expansion cohorts in the Phase I/II trial of AG-221 in hematologic malignancies (H2:14); Another update from AG-221's Phase I dose-escalation trial (ASH 2014); Initial clinical data on AG-120 for IDH1 mutant cancers (2015); Initial clinical data on AG-348 for PK deficiency (2015).

Our Thesis On Agios. Agios is developing AG-221 in collaboration with partner Celgene, which recently picked up its option for exclusive worldwide development rights. IDH2 mutations are thought to affect about 15% of AML and 5% of MDS/MPN; we estimate AG-221 could support peak worldwide sales of $600MM+, on which Agios is entitled to a 10-15% royalty. Meanwhile, Agios is conducting two dose escalation trials for its second candidate, AG-120, targeting IDH1 mutations in liquid and solid tumors. Agios' leading inborn errors of metabolism candidate for orphan diseases is AG-348 for pyruvate kinase deficiency, a rare form of hemolytic anemia. AG-348 is being studied in two Phase I trials (SAD/MAD) in healthy volunteers, with potential proof-of-concept data available in 2015. We are extremely impressed with the early data on AG-221 and expect additional shareholders to accrue as AGIO's targeted oncology and orphan disease programs progress.

Valuation Methodology And Risks

Valuation Methodology

Biotechnology:
In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

Investment Risks

Biotechnology:
There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

Risks To The Price Target

Agios Pharmaceuticals is developing several, currently preclinical, drug candidates in the areas of cancer metabolism and inborn errors of metabolism. All of Agios' drug candidates face clinical and regulatory risk. With the future development path depending on the evolution of clinical data, future revenue forecasts are uncertain. The commercial outlook for Agios' candidates could additionally be altered by safety/efficacy findings, emerging competition, alterations in the medical treatment paradigm, or changes in the pricing environment. Some of Agios' projected market exclusivity depends on patents, which are subject to challenge by generic drugmakers.

Addendum

Stocks Mentioned In Important Disclosures

Ticker	Company Name
AGIO	Agios Pharmaceuticals

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Outperform (1): The stock is expected to achieve a total positive return of at least 15% over the next 12 months

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Assumption: The expected total return calculation includes anticipated dividend yield

Cowen and Company Rating System until May 25, 2013

Outperform (1): Stock expected to outperform the S&P 500

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Underperform (3): Stock expected to underperform the S&P 500

Assumptions: Time horizon is 12 months; S&P 500 is flat over forecast period

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Buy – The fundamentals/valuations of the subject company are improving and the investment return is expected to be 5 to 15 percentage points higher than the general market return

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Cowen And Company Rating Definitions

Distribution of Ratings/Investment Banking Services (IB) as of 03/31/14

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	407	57.08%	85	20.88%
Hold (b)	288	40.39%	8	2.78%
Sell (c)	18	2.52%	1	5.56%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

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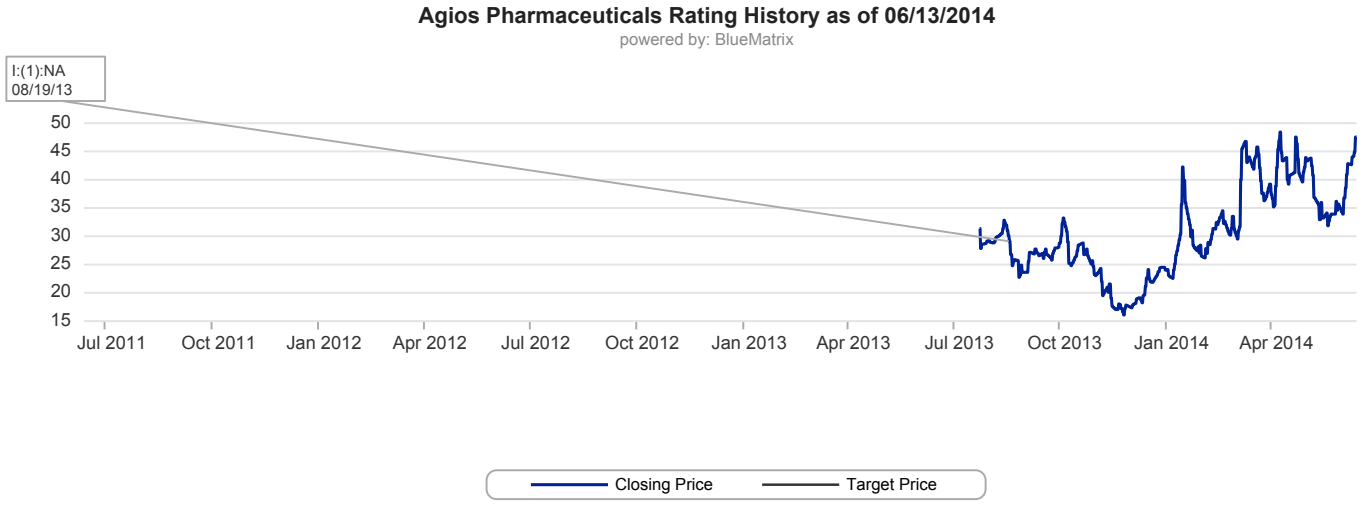

Legend for Price Chart:

I = Initiation | 1 = Outperform | 2 = Market Perform | 3 = Underperform | UR = Price Target Under Review | T = Terminated Coverage | $xx = Price Target | NA = Not Available | S=Suspended

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