Agios Pharmaceuticals

Equity Research

Company Quick Take

June 13, 2014

Price: $44.84 (06/12/2014)

Price Target: NA

OUTPERFORM (1)

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Key Data

Symbol	NASDAQ: AGIO
Market Cap (MM)	$1,522.6

Celgene Opt-In Another Sign Of Confidence In AG-221

The Cowen Insight

Agios announced that partner Celgene has exercised its option (early) on worldwide rights to AG-221, an oral selective inhibitor of mutant IDH2 currently in Phase I/II development for AML. Updated data from the Phase I/II dose-escalation trial will be presented tomorrow at EHA. We expect these results and multiple additional milestones to drive stock outperformance over the next 12-18 months.

The news: As expected, collaboration partner Celgene has exercised its option to gain an exclusive worldwide license to Agio's lead compound AG-221. Celgene had until the end of Phase I to exercise this option, hence the decision came a bit early, likely reflecting Celgene's desire to accelerate development of AG-221 in light of the remarkable early signs of activity observed in the Phase I/II trial. Celgene now has WW development and commercialization rights for AG-221, while Agios has the right to conduct a portion of commercialization activities in the US. Under the terms of the collaboration, Agios is eligible for up to $120MM in milestone payments and a tiered royalty (10-15%) on net sales.

AG-221's Phase I/II dose-escalation trial in patients with IDM2 mutant relapsed or refractory AML or MDS, has produced remarkable single-agent activity and excellent tolerability as shown at the AACR meeting in April. Updated data from the Phase I/II dose-escalation will be presented as an oral late-breaker presentation (Abstract # LB2434) at the EHA meeting on Saturday at 1:30 pm CEST/7:30 am ET.

So what do we expect to see at EHA?

Recall at the AACR presentation, 6 of the 7 evaluable patients had achieved an objective response (86% ORR: 43% CR, 29% CRp, 14% PR) and 5 responding patients remained on study drug. As of April 15, 31 patients have been enrolled in four cohorts; we believe that we could see new data on another 5-10 evaluable patients, beyond what we saw at AACR. We could also see some initial data from the 75mg BID and 100mg QD dose cohorts. Recall that in the data presented at AACR, responses appeared to be developing faster at 50mg BID than 30mg BID and data from high dose cohorts should help determine dose response trends.

Can response rates go any higher?

In light of the 86% response rate reported at AACR, investors are expecting a high rate of response at EHA. However, even a substantially lower rate of response in r/r AML would not change our view that AG-221 is likely to become the standard of care in the IDH2 mutant subpopulation, so investor focus on small changes in the ORR is likely misplaced. We remind investors that our consultants had previously said that a 25% response rate would be impressive for any new agent in a Phase I/II trial for r/r AML, and the data we have seen to date clearly exceed that bar.

Durability of response likely more important.

At EHA, we expect to see further followup on the initial five responders still on drug. These data should begin to shed light on the durability of response. We believe that durability of response, and the ability to get patients to a transplant is likely to be an important gauge of AG-221's ultimate success in r/r AML. However, with the rather limited (~2 month) followup since the AACR presentation, we don't expect to get a lot more visibility on the duration of responses at EHA. A further update, likely at ASH, might provide a more definite answer.

What's next for Agios? Initiate the Phase II expansion cohorts on AG-221 as a monotherapy (H2:14); Initial clinical data on AG-120 for IDH1 mutant cancer (2015); Initial clinical data on AG-348 for PK deficiency (2015).

Our Thesis On AGIO. IDH2 mutations 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 similar dose escalation trials for its second candidate, AG-120, targeting IDH1 mutations in both liquid and solid tumors. Agios' leading IEM candidate is AG-348 for pyruvate kinase deficiency, a rare form of hemolytic anemia, which is currently in two Phase I trials (SAD/MAD) in healthy volunteers, and we would expect proof of concept data in 2015. We applaud the initial clinical success with AG-221 and expect AGIO to continue building long-term value via its targeted oncology and orphan disease programs.

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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Underperform (3): Stock is expected to achieve a total negative return of at least 10% over the next 12 months

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

Neutral (2): Stock expected to perform in line with the S&P 500

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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Hold – The fundamentals/valuations of the subject company are neither improving nor deteriorating and the investment return is expected to be in line with the general market return

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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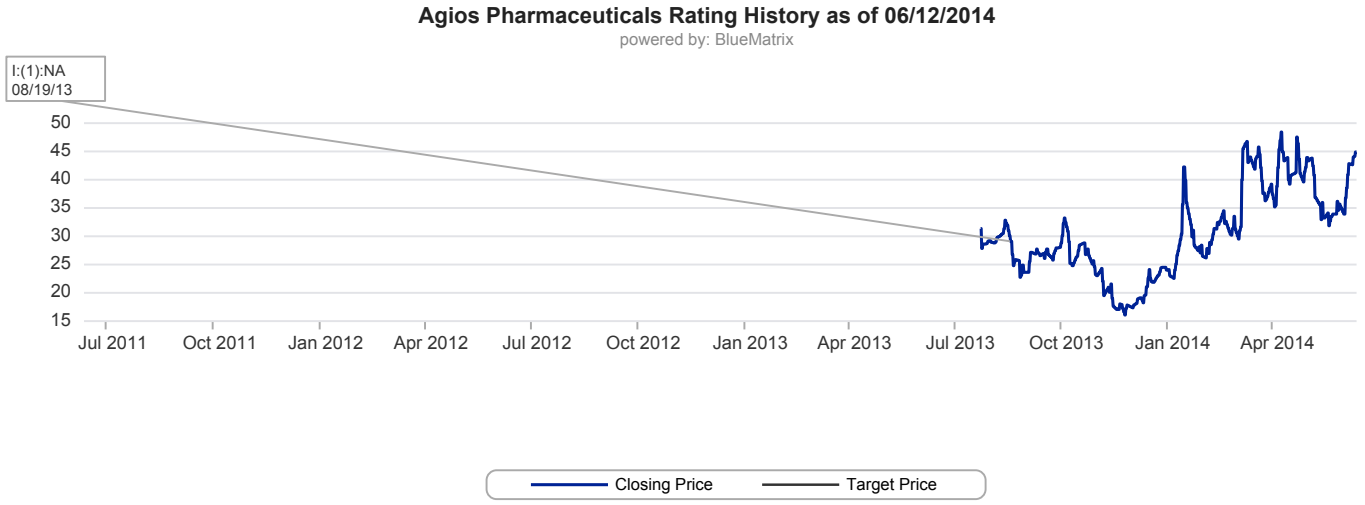

Legend for Price Chart:

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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