# Agios Pharmaceuticals Inc

Equity Research

Company Quick Take

April 7, 2014

**Price: $35.48** (04/4/2014)

**Price Target: NA**

**OUTPERFORM (1)**

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**Key Data**

| | |
|---|---|
| Symbol | NASDAQ: AGIO |
| Market Cap (MM) | $1,120.8 |

## *AG-221's Phase I Trial Data Exceed Expectations*

### The Cowen Insight

Yesterday, at the AACR meeting in San Diego, Agios reported the first clinical data from the Phase I dose escalation trial of its lead candidate, AG-221 for IDH2-mutant (IDH2m) AML. The remarkable single-agent activity and excellent tolerability suggest that Agios may have a drug on its hands, and prove the value of Agios' metabolic platform. We expect the stock to be up sharply this morning.

Agios reported interim data from a Phase I single-agent dose escalation trial of AG-221. (Recall this drug previously showed strong preclinical data; see our note from ASH 2013). AGI-221's Phase I trial enrolled patients with IDH2m, relapsed or refractory AML or MDS. At the data cutoff of March 20, 2014, the trial had enrolled 22 patients in five dose cohorts (30 mg BID, 50 mg BID, 75 mg BID, and 100 mg QD); the MTD has not been achieved and dose escalation continues. 16 patients remain on study (4 died of leukemia-related infection, 1 was transplanted, and one failed to respond and went off study).

At baseline, patients had high risk characteristics; for perspective, the physician presenter remarked that he would guess that only 10% might survive one year on standard treatments. It is thus remarkable that 6 of 7 evaluable patients in the first 10 enrolled (the 30 mg cohort and the 50 mg cohort) responded, an 86% ORR (43% CR, 29% CRp, 14% PR). Moreover, responses seemed to appear earlier in therapy at the higher doses (about the 4th or 5th cycle at 30 mg BID, but the 2nd or 3rd cycle at 50 mg BID). Our consultants had previously said that a 20-25% response rate would be impressive for any new agent in a Phase I trial for AML, so these data clearly exceed that bar.

Safety was also good: among the safety population (n = 22), there were no DLTs and just two SAEs (one Grade 2 hyperleukocytosis and differentiation syndrome, and one Grade 3 confusion in the context of septic shock and respiratory failure, and thus difficult to attribute to the drug).

Further evidence suggested that AG-221 is likely working by the mechanism elucidated preclinically. The oncometabolite and biomarker, 2-HG, was suppressed by over 90%. This would be expected to release a differentiation block, and consistently, in all responding patients blast counts declined and normally differentiated neutrophil counts increased.

Agios plans to continue dose escalation on AG-221 to define the MTD, and will also begin Phase II expansion cohorts this year. The biggest unanswered question is on duration of response, though physicians suggest that even the 2 months (and counting) seen with responses so far is impressive. Possible forums for data updates include EHA (June) and ASH (December). 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 last month initiated two similar dose escalation trials for its second candidate, AG-120, targeting IDH1 mutations in both liquid and solid tumors, and plans to initiate a clinical trial in a third candidate, AG-348 for the orphan disease Pyruvate Kinase Deficiency in mid-2014. We applaud the initial clinical success with AG-221 and expect AGIO to continue building long-term value via its metabolic medicine platform.

# *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 Inc |

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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

**Market Perform (2):** The stock is expected to have a total return that falls between the parameters of an Outperform and Underperform 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

**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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| 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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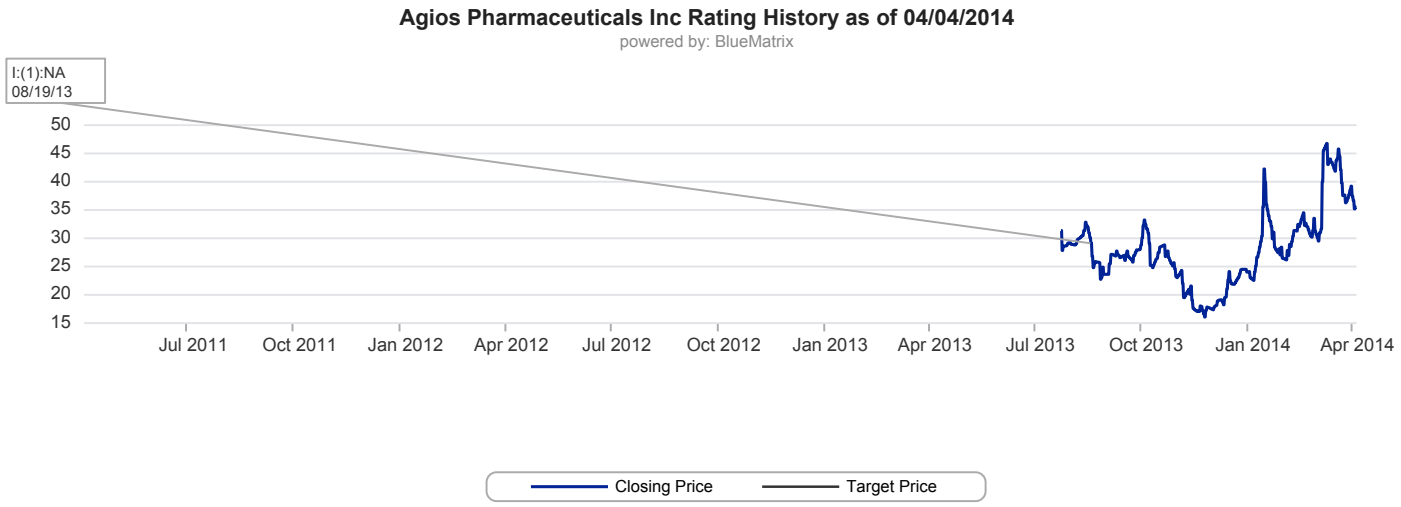


**Legend for Price Chart:**

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

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