COWEN
AND COMPANY

Biotechnology

Agios Pharmaceuticals Inc

Equity Research

Company Quick Take

December 11, 2013

Price: $18.67 (12/10/2013)
Price Target: NA

OUTPERFORM (1)

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New Data And Management Commentary From ASH

The Cowen Insight

We attended Agios' ASH presentation of preclinical data on its lead drug, AGI-221, which targets IDH2-mutant cancer. The data presented indicate strong efficacy for AGI-221 and are supportive of Agios' proposed mechanism of action. The new data, and our conversations with management afterward, bolster our confidence in the ongoing Phase I trial.

New Preclinical Data Consistent With Agios' Proposed Drug Mechanism...

Agios gave an oral presentation showing AG-221's efficacy in a preclinical AML model. Primary IDH2-mutant human leukemia samples are implanted into irradiated mice, resulting in engraftment, frank leukemia within 40 days, and death within 80 days. The leukemic cells can be identified by the cell surface marker, human CD45, though they do not express CD15, a marker of more differentiated cells. Agios treated the mice when they reached ~10% blasts in the peripheral blood, to address disease treatment rather than prevention.

Agios had previously disclosed that single-agent AG-221 treatment in this system caused a dose-dependent increase in survival, reaching 100% at the highest dose, while AraC had a minimal effect on survival. The ASH data reported many details consistent with Agios' proposed mechanism of action for AGI-221, which is that AGI-221 reverses a 2-HG-mediated differentiation block in the leukemic cells. New datapoints included: (1) 2-HG levels rose with parallel kinetics to the leukemic cells in the blood; (2) treatment with AG-221, but not AraC, caused an initial "proliferative burst" of human cells in the blood (consistent with differentiation) followed by a decline of leukemic cells; (3) treatment with AG-221, but not AraC, induced expression of the differentiated cell marker CD15; and (4) AGI-221, but not AraC, caused morphological appearance of differentiated cells in previously 100% blastic bone marrow. Management noted the bone marrow slides were evaluated by blinded, off site pathologists, as they will be in the ongoing Phase I trial.

...And Raise Our Confidence For The Phase I Trial.

AGI-221 is currently in a Phase I dose escalation trial. Management is pleased with the speed of enrollment and suggests data may be available in H2:14, depending on number of cohorts required. In management's view, AGI-221's therapeutic window is likely wide, so the main question is whether it will be once or twice-daily. Management is unconcerned about the "proliferative burst" seen in the ASH data, as this is consistent with the proposed mechanism, and also occurs in ATRA-treated APML, where it can be easily managed by watchful waiting or hydroxyurea. Management is hopeful for sufficient single-agent activity to register AGI-221, but expects the drug to be even more powerful in combination, perhaps with chemo or with other targeted agents (such as Bcl2 inhibitors (e.g. ABT-199) or Flt3 inhibitors (e.g. quizartinib)).

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 regualtory 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

Analyst Certification

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Cowen and Company Rating System effective May 25, 2013

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

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

Cowen Securities, formerly known as Dahlman Rose & Company, Rating System until May 25, 2013

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 09/30/13

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	394	58.72%	54	13.71%
Hold (b)	255	38.00%	5	1.96%
Sell (c)	22	3.28%	1	4.55%

(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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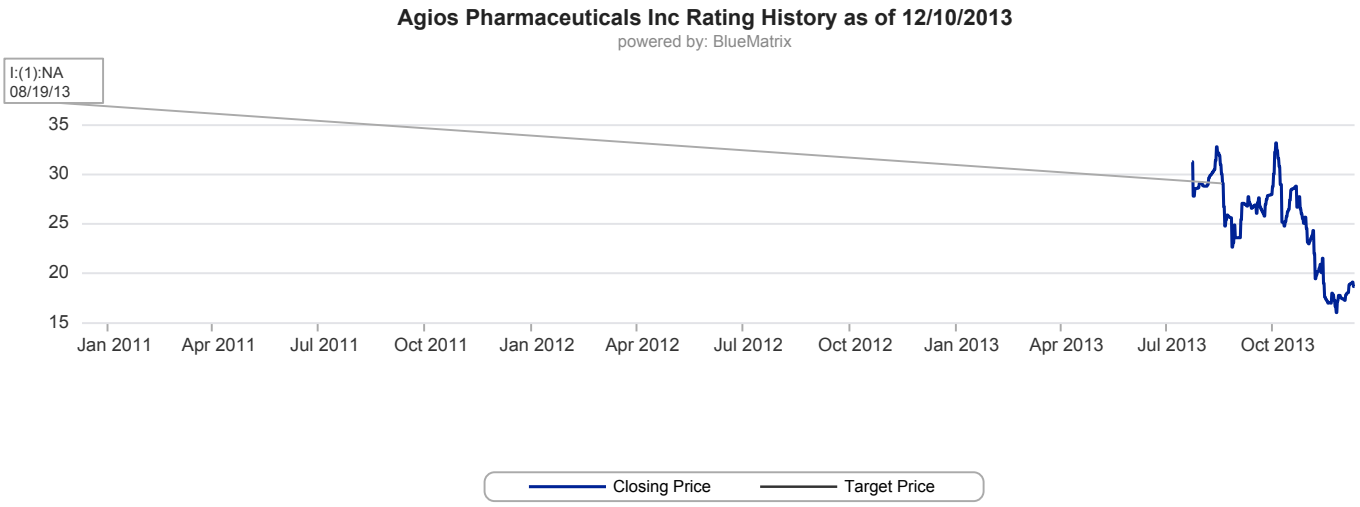

Legend for Price Chart:

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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