

Agios Pharmaceuticals

Interim Phase 1 AG-221 Impressive; CRs an Upside Surprise - ALERT

We are attending the AACR meeting (San Diego) where interim phase 1 data for AG-221 in advanced hematologic malignancies were press released by Agios. Overall, in our view, these initial data were very robust and well ahead of our / Street expectations, with 6/7 patients achieving a clinical response (see details below). Indeed, proof-of-concept has definitively been established, in our view. We note that expectations going into the meeting were for perhaps 1-2 responses, which did raise the bar but were clearly exceeded. Importantly, we believe these data validate not only AG-221 but also the broader oncology development program (i.e., AG-120), as well as the company's technology platform. The full phase 1 interim data will be presented later today at 3:45pm PST.

- **Efficacy – 2HG declines in line with expectations...** It was noted that there was meaningful reduction of 2-HG, which does not come as a surprise, in our view. Recall, pre-clinical data at ASH 2013 showed that AG-221 was associated with rapid decline in 2-HG. Of note, PK analysis showed that mean plasma half-life of >40 hours for both the 30mg and 50mg doses. As such, Agios is evaluating both 1x and 2x/day dosing regimens going forward.
- **...but responses, a major upside surprise:** Data from the first 2 cohorts (30mg and 50mg BID; n=10 all R/R AML) of the phase 1 trial showed that 6/7 patients objective responses, including 3 patients with CRs, 2 patients with CRs but with incomplete platelet recovery, and 1 patient with a PR. Of note, 1 patient with a CR went to transplant and death occurred in 3 patients, all in the first cohort (did not finish full cycle of therapy). In our view, the clinical responses were a major upside surprise and were well ahead of Street expectations.
- **Key safety takeaways:** Limited safety details were provided. It was noted that no dose limited toxicities have been observed and that AG-221 has been well-tolerated to date. Of note, possible drug related SAEs included elevated white blood cell count in a single patient and confusion / respiratory failure in another patient that had disease related infection.
- **What we are looking for in the presentation later today:** Our focus will be on additional details on the safety profile, particularly on commentary related to possible drug SAEs. On the efficacy side, our focus will be on how quickly 2-HG declined and additional details on when responses occurred during treatment and commentary on durability of response.
- **Maintain Neutral Rating.**

Neutral

AGIO, AGIO US

Price: \$35.48

04 April 2014

Biotechnology

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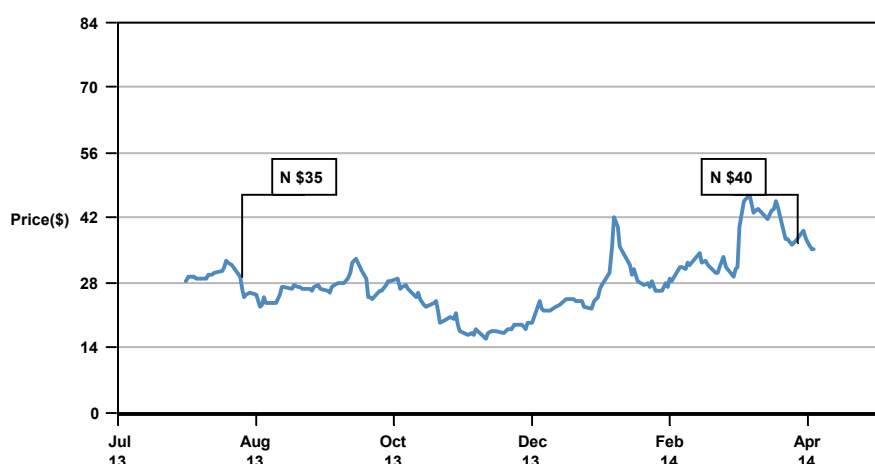
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Agios Pharmaceuticals (AGIO, AGIO US) Price Chart



Date	Rating	Share Price (\$)	Price Target (\$)
19-Aug-13	N	29.11	35.00
28-Mar-14	N	36.56	40.00

Source: Bloomberg and J.P. Morgan; price data adjusted for stock splits and dividends.
Initiated coverage Aug 19, 2013.

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