June 16, 2014

OUTPERFORM

Reason for report:

COMPANY UPDATE

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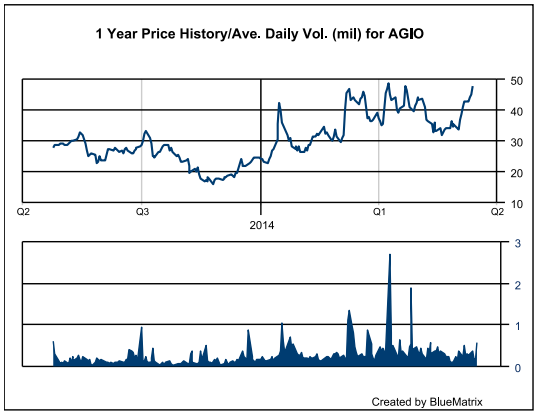
AGIOS PHARMACEUTICALS, INC.

AG-221 EHA Update Provides Initial Evidence of Durability and Activity in MDS

• **Bottom Line:** At the ongoing European Hematology Association (EHA) meeting, updated data from the AG-221 (IDH2 mutant inhibitor) Phase I trial on 25 evaluable patients with IDH2-mutated acute myeloid leukemia (AML) (compared to 7 for presentation at the AACR in April) provided the initial evidence of durability of responses with no relapse to date in any of the 14 responders and 5 complete responses (CR) durable for at least 2.5 months and up to 4 months. In addition, activity has been has been observed beyond AML and all 4 myelodysplastic syndrome (MDS) patients have responded to date. While the duration of response data are still early, given that a response of 2.5+ to 4+ months is likely already meaningful for AML, we believe the initial evidence on durability adds an important datapoint to the drug's profile and suggests that this so-far well tolerated oral drug could provide a meaningful benefit in a substantial portion of patients. As response on AG-221 appears to deepen over time and the IDH2 mutation status of the patients is still being verified, response rate data could change and possibly improve as data mature (next update likely at ASH). We maintain our $65 price target.

• **Clinical as well as biochemical response seen at the lowest dose.** Data presented at the AACR showed overall responses in 6 out 7 evaluable patients and CRs in 3/7 patients at 30mg and 50mg BID doses. The updated data showed objective response from 14 out of 25 evaluable patients (6 CRs, 2 CRp [CR with incomplete platelet recovery] and 1 CRi [CR with incomplete hematologic recovery], and 5 partial responses [PR]) with additional 5 stable diseases (SDs) which could still develop into PR or CR with longer treatment duration based on the response pattern in other patients. So far 6/25 had progressive disease (PD) and none of the 14 responders had relapsed and two were off study drug for reasons not related to the drug (1 for bone marrow transplant and another died from surgical complications after a traumatic accident). With additional patients added to both of two lowest dose cohorts, activity continues to be seen at these doses (4/4 response at 30 mg BID and 5/7 mg BID). In addition, substantial reductions in plasma levels of the oncometabolite 2-hydroxyglutarate (2HG) was seen at all dose levels including the lowest dose. Therefore evidence of strong clinical and biochemical activity was seen even at the lowest level although management noted that at higher doses the onset of responses appears more rapid. Responders at the two lowest doses include both responses with R172K mutation (10-15% of IDH2 mutations) for which AG-221 appears to have less in vitro activity (the remainder of the 14 responders had R140Q mutation). Activity of AG-221 was seen beyond AML and four patients with MDS all responded to AG-221 including 1 CR, 1 CRp and 2 PRs.

Key Stats:	**(NASDAQ:AGIO)**
S&P 600 Health Care Index:	**1,282.26**
Price:	**$47.50**
Price Target:	$65.00
Methodology:	NPV + $500M for Platform / Pipeline + Cash
52 Week High:	$49.79
52 Week Low:	$15.77
Shares Outstanding (mil):	33.9
Market Capitalization (mil):	$1,610.3
Book Value/Share:	$0.14
Cash Per Share:	$7.54
Dividend (ann):	$0.00
Dividend Yield:	0.0%
Cash Per Share: Pro forma	



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2013A	$6.3	$6.3	$6.3	$6.7	$25.5	($0.39)	($2.80)	($0.52)	($0.40)	($2.83)	NM
2014E	$8.4A	$2.8	$5.5	$5.5	$22.1	($0.39)A	($0.55)	($0.49)	($0.51)	($1.95)	NM
2015E	--	--	--	--	$7.3	--	--	--	--	($2.38)	NM

Source: Company Information and Leerink Partners LLC Research
Revenues in millions.
2013 Q3 10Q reported ($0.47) in EPS. However, we believe the correct EPS should be ($0.52) due to calculation error with cumulative preferred stock dividends.

INVESTMENT THESIS

AGIO's strong platform in cellular metabolism has resulted in seminal discoveries which the company has been able to capitalize and translate into a full array of early clinical or late-preclinical pipeline agents targeting cancer and ultra-orphan indications of inborn errors of metabolism (IEMs). AGIO is a clear leader in the discipline of cancer metabolism, a potentially fruitful area of exploration for new cancer therapeutics. AGIO's most advanced candidates AG-221 and AG-120 targeting mutations in the enzymes isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2). Both targets are genetically validated and mutations have been identified in acute myeloid leukemia, brain cancer, sarcoma, and biliary tract cancers. Third candidate AG-348 targets the ultra-orphan blood disorder of pyruvate kinase deficiency which is an IEM manifested by severe hemolysis. Although we are clearly mindful that AGIO's pipeline is very early, there is very strong genetic validation for the lead candidates. The observations of single mutation in IDH1 and IDH2 (isocitrate dehydrogenase) on a single allele being associated with cancer point to gain of function alterations that are well suited for drug therapeutics. As AGIO pioneered the field, there does not appear to be visible competition. AGIO's strong partnership with CELG (OP) not only funds the programs but also leaves good upside including full US rights for 1 in 3 compounds. These terms, based purely on the cancer metabolism platform with compounds still on the drawing board, are impressive and in our view provide clear validation for AGIO. Additionally, AGIO is leveraging its metabolism platform to target rare IEMs that we believe could provide a rapid path to market. Its lead IEM compound AG-348, appears to be able to accomplish the difficult task of activating multiple defective forms of pyruvate kinase-R and potentially provides a therapy for pyruvate kinase deficiency (PKD), a rare blood disorder.

Toxicity profile remains favorable, maximal tolerated dose (MTD) not reached yet. With a total of 35 patients dosed, longer follow up and higher dosing regimens, MTD still has not been reached yet. Most toxicities were Grade 1/2 and related to the AML disease. There were possibly drug-related SAEs in four patients including confusion, respiratory failure, leukocytosis, anorexia, nausea and diarrhea. There were 7 deaths but unrelated to the drug.

Phase II dose not finalized, mutation profile under validation, extension cohorts to further evaluate AG-221 activity. Given activities seen at 30mg dose, more patients were added to the 30mg cohort. However, final dose for Phase II is still not decided yet. So far, not all mutations have been identified and all tissues have been sent to Foundation Medicine (OP) for final sequencing. Additionally, given initial promising activity, AGIO plans to enroll 100 patients in the extension cohorts in 2H:14 with 25 in each of four cohorts – R/R AML of 60 years and older, R/R AML less than 60 years old, front line AML who declined standard of care, and patients with other IDH2 mutations. Partner CELG has exercised option to in-license AG-221 early and it appears likely that AG-221 could be moved into accelerated development.

AG-221 Phase I Data at AACR and EHA

AACR 2014	30 mg BID	50 mg BID	Total
n =	5	5	10
n evaluable	**2**	**5**	**7**
CR	1	1	3
CRp	1	1	2
PR		1	1
PD		1	1
NE	3	0	3
ORR	**2/2**	**4/5**	**6/7**

EHA 2014	30 mg BID	50 mg BID	75 mg BID	100 mg QD	100 mg BID	150 mg QD	Total
n evaluable	**4**	**7**	**4**	**5**	**3**	**2**	**25**
CR	2	3		1			6
CRp	1				1		2
CRi		1					1
PR	1	1	1		1	1	5
SD		1	2	1		1	5
PD		1	1	3	1		6
ORR	**4/4**	**5/7**	**1/4**	**1/5**	**2/3**	**1/2**	**14/25**

Note: AACR – American Association for Cancer Research; EHA – European Hematology Association; BID – twice daily; QD – once daily; CR – complete response; CRp – complete response with incomplete platelet recovery; CRi – complete response with incomplete blood count recovery; PR – partial response; SD – stable disease; PD – progression disease; NE – not evaluable

Source: Company reports and Leerink Partners LLC

AGIO Upcoming Catalysts

Compound	Timing	Event
AG-221 (IDH2)	ASH 2014	Update from Phase I dose escalation study in hematologic malignancies with IDH2 mutations
	2H:14	Initiating Phase I expansion cohorts
AG-120 (IDH1)	Medical conferences in 2015	Initial data from two Phase I trials in solid tumor and hematologic malignancies with IDH1 mutations
AG-348 (PKR activator)	Medical conferences in 2015	Interim data from Phase I dose escalation study in healthy volunteers

Source: Company reports and Leerink Partners LLC

AGIO Product Pipeline

Drug	Status	Note
AG-221 (IDH2 inhibitor)	Phase I	Phase I dose escalation study in IDH2m hematologic malignancies initiated in 3Q:13.
AG-120 (IDH1 inhibitor)	Phase I	Phase I trials in solid tumor and hematologic malignancies initiated in 1Q:14
AG-348 (PKR activator)	Phase I	Phase I trial in healthy volunteer initiated in 2Q:14

Source: Company reports and Leerink Partners LLC

VALUATION

Our $65 price target for AGIO is based on NPV and sum of the parts methodology. Our probability of success is 70% for AG-221 (IDH2), 40% for AG-120 (IDH1), and 15% for AG-348 (PKD). We use a 10% discount rate and believe it is appropriate given probability weighted sales projections. Our royalty assumption is 10-13% for IDH2 w/w sales and IDH1 Ex-US sales. We include $500M valuation for the platform and other pipeline and estimated $240M cash.

RISKS TO VALUATION

- All pipeline assets are still in early-stage clinical or preclinical development and many hurdles remain.
- AGIO's agents have been all first-in-class. Clinical toxicity and efficacy of Agios compounds as well as proof of principle remain to be established.
- Additional funding will be required before turning profitable.

AGIO Income Statement	2011A	2012A	2013A	Mar-14A	Jun-14E	Sep-14E	Dec-14E	2014E	2015E	2016E	2017E
Collaboration agreements											
Royalties											
Sales											
Total revenue	21,837	25,106	25,548	8,411	2,818	5,454	5,454	22,137	7,272	0	0
COGS											
% of revenue											
R&D	31,253	41,037	54,502	17,407	18,103	18,827	19,581	73,918	76,136	78,420	80,772
G&A	7,215	7,064	9,929	3,288	3,321	3,354	3,388	13,351	14,686	16,154	17,770
% of revenue											
Total operating expenses	38,468	48,101	64,431	20,695	21,424	22,182	22,968	87,269	90,821	94,574	98,542
Net income (loss) from operations	(16,631)	(22,995)	(38,883)	(12,284)	(18,606)	(16,728)	(17,514)	(65,132)	(83,549)	(94,574)	(98,542)
Investment income	132	69	55	36	0	0	0	36	0	0	0
Net income (loss) before income taxes	(16,499)	(22,926)	(38,828)	(12,248)	(18,606)	(16,728)	(17,514)	(65,096)	(83,549)	(94,574)	(98,542)
Provision (benefit) for income taxes	7,207	(2,824)	579	0	0	0	0	0	0		
Tax rate											
Net income (loss)	(23,706)	(20,102)	(39,407)	(12,248)	(18,606)	(16,728)	(17,514)	(65,096)	(83,549)	(94,574)	(98,542)
Cumulative preferred stock dividends	(3,100)	(7,190)	(4,162)	0	0	0	0	0	0		
Net income (loss) to common stockholders	(26,806)	(27,292)	(43,569)	(12,248)	(18,606)	(16,728)	(17,514)	(65,096)	(83,549)	(94,574)	(98,542)
Net loss per share	**(8.90)**	**(1.18)**	**(2.83)**	**(0.39)**	**(0.55)**	**(0.49)**	**(0.51)**	**(1.95)**	**(2.38)**	**(2.57)**	**(2.55)**
Basic shares	3,013	23,133	15,415	31,395	33,852	34,021	34,191	33,365	35,033	36,785	38,624
Dilutive shares			27,724	33,813	36,283	36,464	36,646	35,802	37,592	39,471	46,445

Source: Company Reports and Leerink Partners

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Disclosures Appendix

Analyst Certification

I, Howard Liang, Ph.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

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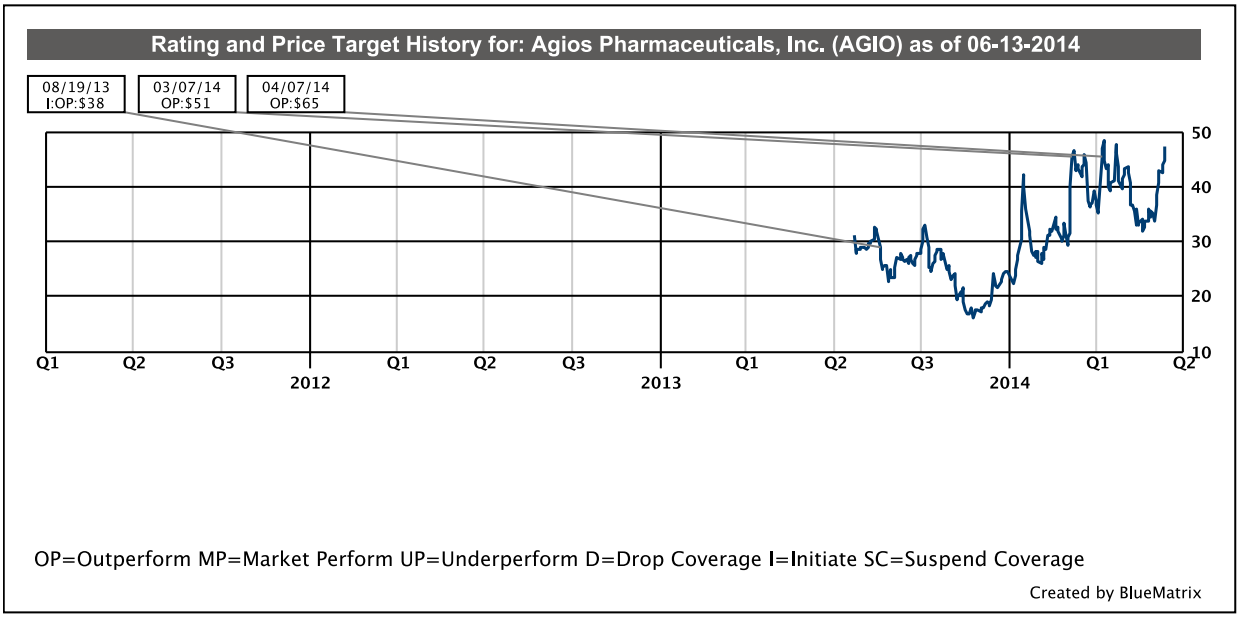
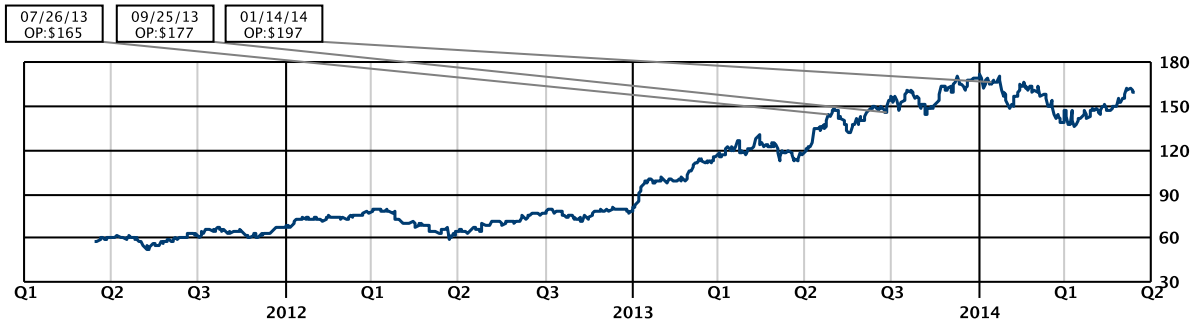


Rating and Price Target History for: Celgene, Inc. (CELG) as of 06-13-2014

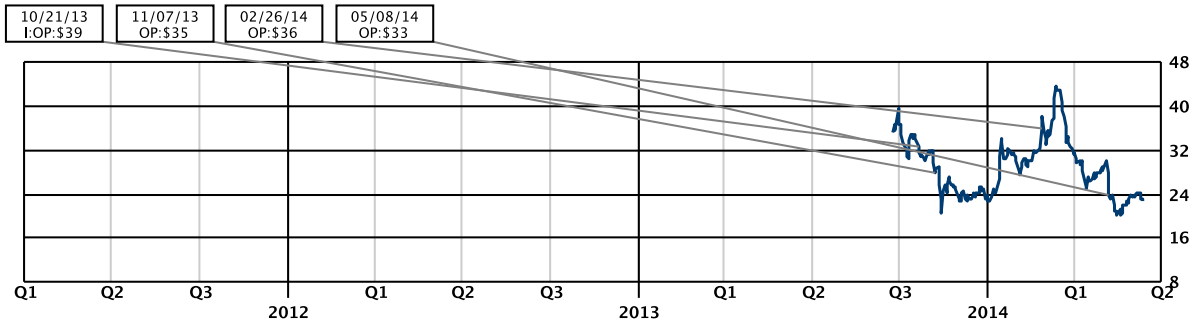


Leerink Swann initiated coverage of CELG with an Outperform rating on February 7, 2003. On June 11, 2013, Leerink Swann began a transition to specific price targets for the stocks under its coverage, replacing valuation ranges.

OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

Created by BlueMatrix

Rating and Price Target History for: Foundation Medicine, Inc. (FMI) as of 06-13-2014



OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

Created by BlueMatrix

Distribution of Ratings/Investment Banking Services (IB) as of 03/31/14				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	131	68.23	46	35.11
HOLD [MP]	61	31.77	3	4.92
SELL [UP]	0	0.00	0	0.00

Explanation of Ratings

Outperform (Buy): We expect this stock to outperform its benchmark over the next 12 months.

Market Perform (Hold/Neutral): We expect this stock to perform in line with its benchmark over the next 12 months.

Underperform (Sell): We expect this stock to underperform its benchmark over the next 12 months.The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than $2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over $2 billion.

Important Disclosures

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In the past 12 months, the Firm has received compensation for providing investment banking services to Agios Pharmaceuticals, Inc. and Foundation Medicine, Inc. .

Leerink Partners LLC makes a market in Agios Pharmaceuticals, Inc., Celgene, Inc. and Foundation Medicine, Inc.

Leerink Partners LLC has acted as a co-manager for a public offering of Agios Pharmaceuticals, Inc. and Foundation Medicine, Inc. in the past 12 months.

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