May 22, 2015

OUTPERFORM

Reason for report:

FLASH NOTE

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LEERINK

CALITHERA BIOSCIENCES, INC.

Demonstration of Initial Single-Agent Activity Provides Support for MOA

Key Stats:	(NASDAQ:CALA)
S&P 600 Health Care Index:	**1,660.54**
Price:	**$12.02**
52 Week High:	$33.48
52 Week Low:	$6.51
Shares Outstanding (mil):	17.9
Market Capitalization (mil):	$215.2

• **Bottom Line:** Abstracts for the 2015 European Hematology Association (EHA) Congress in Vienna, Austria (June 11-14), were released yesterday, including new data for CALA's glutaminase inhibitor CB-839. The finding of a complete response in the bone marrow of an AML patient with single-agent CB-839 provides for the first time clear evidence of clinical activity of CALA's lead compound, after the firm had previously reported only stable disease as the best response in the Phase I solid tumor trial (data to be presented at ASCO). Although it is not clear at what dose each of the AML patients was treated (the press release and abstract state patients received between 100 and 1000 mg three times daily), we are also very encouraged that a therapeutic dose was reached without any significant safety signals, which is in line with the previously reported results from solid tumors. Although one would generally like to see more than a single response, we believe the first report of an objective response is highly encouraging as it provides support for the mechanism of action (MOA). The question for CB-839 in AML will become one of the frequency of the response, and there is a possibility that the response rate could be higher at the therapeutic dose (assuming the response was seen at one of the higher doses). Based on our understanding of the biology, we continue to believe the activity of glutaminase inhibitors could be context-dependent and there could be opportunities to enhance activity through patient selection or combination.

• **CALA's lead product CB-839 shows single-agent clinical activity in AML.** Calithera Biosciences is presenting first results from its Phase I study of lead product CB-839 (glutaminase inhibitor) in acute leukemias in abstract #E947, having previously disclosed results from its Phase I solid tumor study in an ASCO abstract and press release. Of 15 treated and evaluable patients as of the data cutoff (March 1, stated in press release), all of whom had AML, single-agent CB-839 produced a complete response in the bone marrow with incomplete recovery of peripheral counts (CRi) in one patient. In addition, 5 patients (33%) saw stable disease lasting for 4 to 10 cycles (each cycle consisting of 3 weeks of treatment). The abstract also implies that the number of patients to be enrolled into the expansion cohort in AML is contingent on seeing clinical responses, and that the observed CRi triggered enrollment of additional patients. No dose-limiting toxicities were seen, and treatment-related toxicities were generally low-grade and infrequent. The pharmacokinetic data reported seem to track well with those in the solid tumor trial and continue to support 600 BID dosing based on serum exposure.

• **The initial demonstration of single-agent activity could be significant in light of the concern about glutaminase as a target.** There have been lingering concerns about whether glutaminase inhibition would be capable of single-agent clinical activity, because tumors may be able to change their metabolic dependence away from glutamine, thus circumventing the effect of the drug. Notably, AGIO (OP) recently formally announced stopping a glutaminase inhibitor program (which remained preclinical), citing lack of observed single-agent activity in mouse studies. The fact that CALA saw a single-agent complete response, particularly in

a patient group that had not been selected for genetic mutations related to glutamine metabolism, provides an important initial validation of the underlying mechanism, in our view.

Disclosures Appendix

Analyst Certification

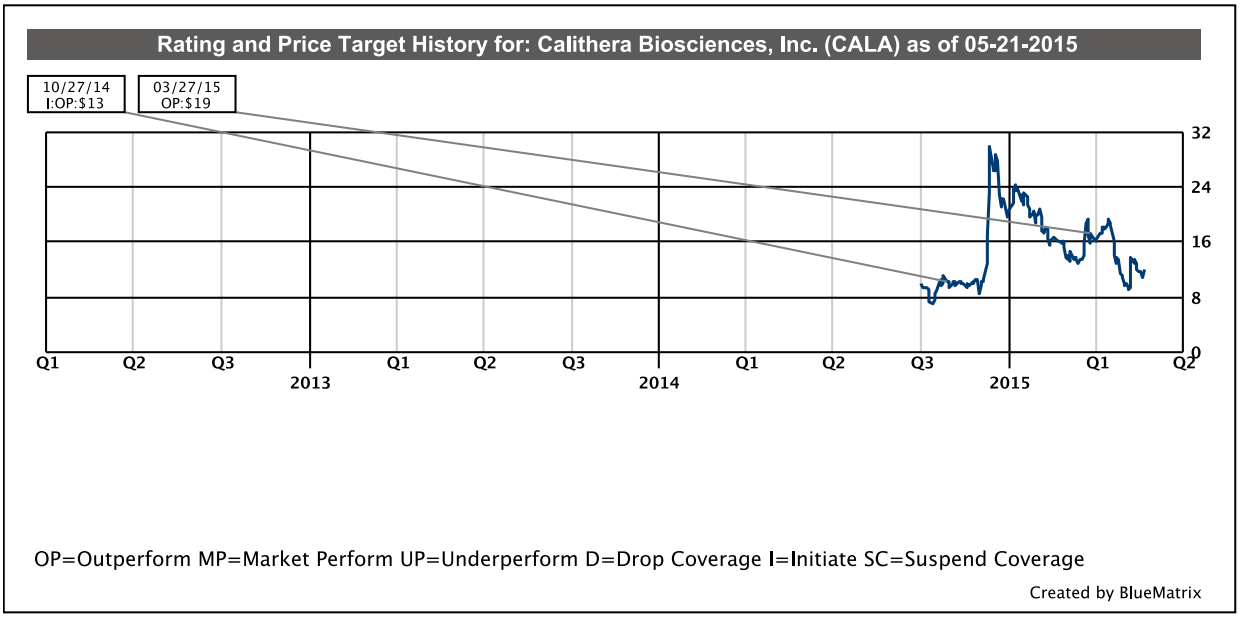
I, Howard Liang, Ph.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

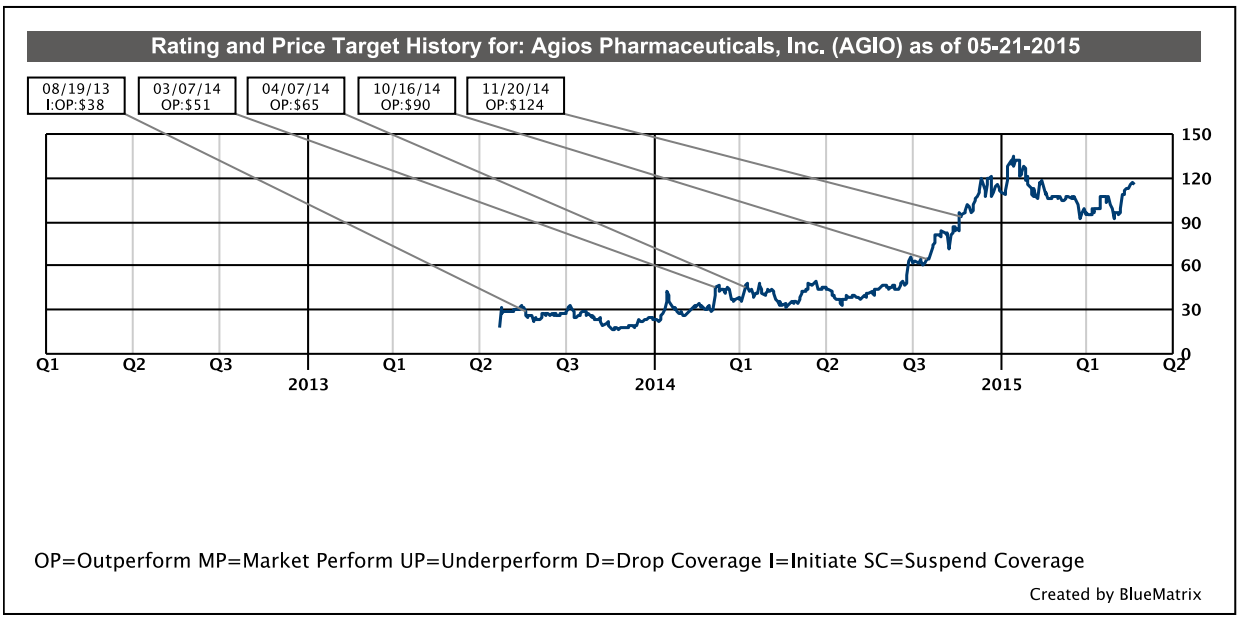
Valuation

Our $19 valuation for CALA is based on a DCF analysis and probability-weighted sales for CB-839 in triple-negative breast cancer (TNBC) and multiple myeloma (MM) with a probability of success of 15% for both indications. We use a 10% discount rate, which we believe is appropriate, as our valuation uses probability-weighted sales.

Risks to Valuation

Risks to our valuation include clinical, regulatory, commercial, and competitive risks for pipeline products. CALA's clinical programs are still at a relatively early stage, therefore significant uncertainties exist. As a development-stage company several years away from a commercial launch, there are also financing risks.




Rating and Price Target History for: Agios Pharmaceuticals, Inc. (AGIO) as of 05-21-2015
08/19/13
I:OP:$38
03/07/14
OP:$51
04/07/14
OP:$65
10/16/14
OP:$90
11/20/14
OP:$124
150
120
90
60
30
0
Q1
Q2
Q3
2013
Q1
Q2
Q3
2014
Q1
Q2
Q3
2015
Q1
Q2
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 03/31/15				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	151	70.20	55	36.00
HOLD [MP]	64	29.80	2	3.00
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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Leerink Partners LLC has acted as a co-manager for a public offering of Agios Pharmaceuticals, Inc. in the past 12 months.

Leerink Partners LLC has acted as the manager for a public offering of Calithera Biosciences, Inc. in the past 12 months.

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