Equity Research

Company Quick Take

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Price: $26.09 (06/13/2014)

Price Target: NA

OUTPERFORM (1)

Eric Schmidt, Ph.D.
646.562.1345
eric.schmidt@cowen.com

Key Data

Symbol	NASDAQ: BLUE
Market Cap (MM)	$639.5

Two For Two: A Great Start In Beta-Thalassemia

The Cowen Insight

At EHA, bluebird presented initial data from its Phase I/II HGB-205 study on LentiGlobin gene therapy for beta-thalassemia. The first two patients on the trial rapidly obtained transfusion independence, suggesting BLUE's new BB305 vector offers superior potency. BLUE also presented follow up data on the earlier generation vector that supports durability of transgene expression out to 6 years.

Rapid Transfusion Independence Achieved In Initial Two Patients

On Saturday at the 19th EHA Congress, bluebird presented data on the first two patients treated in its HGB-205 trial in beta-thalassemia patients. Recall bluebird is testing its LentiGlobin gene therapy in two Phase I/II studies (HGB-205 in France, Northstar in the U.S.) using a modified and hopefully more potent BB305 vector. HGB-205 is a follow-on trial to LG001, an academic study that utilized an older version LentiGlobin vector, HPV569. The HGB-205 and Northstar trials are designed to enroll up to n=7 (including some patients with sickle cell disease) and n=15 patients (all beta thalassemia), respectively.

While it is still early in the conduct of HGB-205 (only 2 patients treated with follow up of 2-4.5 months), the trial has already produced compelling proof-of-concept efficacy, and data to indicate that the new BB305 vector offers superior potency relative to the prior generation construct. Advantages of the next generation vector appear to include:

-*Better transduction efficiency*. Vector copy number, a measure of in vitro transduction efficiency, was approximately 3x higher in the two patients treated with BB305. Reported VCN were 1.5 and 2.1 for the BB305 patients versus 0.6 and 0.3 for the HPV569 patients.This could in part be a function of selection, as patients in HGB-205 are required to have a minimal copy number prior to transplantation.

-*Faster engraftment times*. Patients in HGB-205 witness faster stem cell engraftment (Day 13 and 15 vs. Day 29 and 20). This could be a function of the higher number of CD34+ cells transplanted or lower inherent toxicity associated with the vector (that makes cells more viable). Either way, faster engraftment times benefit patients in terms of lesser infectious and other risks.

-*Higher hemoglobin production*. bluebird monitors Hb production in vivo by measuring the amount of T87Q (transgenic) protein produced. Subjects in HGB-205 produced 6.6 g/dL and 4.2 g/dL of T87Q protein at 4.5 and 2 months follow-up, respectively. This is well over 10x higher than in the prior trial.

-*Improved outcomes*. Both patients treated in HB-205 achieved transfusion independence by day 12. Both patients remain transfusion independent 3 and 6 months post procedure. In contrast, one of 4 patients treated in the LG001 study achieved transfusion independence, and not until 12 months post procedure. The

good news is that this patient remains transfusion independent ~6 years post transplant, indicating good durability of effect once transgene expression takes place.

Recall that bluebird's ongoing and potentially pivotal CCALD trial also employs the new BB305 vector. Hence the advantages in efficiency, potency and speed of onset relative to prior generation vectors might also be observed in this study.

Safety Continues To Look Good; Next Update In Late 2014

No drug product related AEs have been reported in the HGB-205 trial, or LG001 study, which is now going on five years. In addition, an integration site analysis of the first subject treated in HGB-205 showed a polyclonal reconstitution, which suggests a lower probability for safety issues down the road. Obviously, additional patients and longer-term follow up will be needed to better establish the safety of LentiGlobin. bluebird reports that one patient has been treated in the Northstar trial and that a total of 10 have been enrolled across HGB-205 and Northstar. The next update from these studies is anticipated in late 2014.

Our Thesis On BLUE

bluebird bio seeks to provide transformative one-time gene therapy-based treatments to patients with severe orphan diseases. The company has generated proof-of-concept data in two genetic conditions: childhood cerebral adrenoleukodystrophy (CCALD), an X-linked disorder of progressive neurodegenerative decline, and beta-thalassemia, an autosomal recessive disease of red blood cell dysfunction characterized by severe anemia. These programs are de-risked by early clinical proof of concept studies, and bluebird retains full ownership to these programs. We view CCALD as a potential $100-200MM opportunity and beta-thalassemia as a potential $500-$1B opportunity. A separate, earlier stage collaboration with Celgene based upon chimeric antigen receptor (CAR) T cells is aimed at cancer. We expect multiple value creating milestones to drive stock outperformance.

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

bluebird bio has no approved products and limited revenue. The company may need to raise additional capital from the public markets prior to turning profitable. bluebird's two lead candidates (Lenti-D and LentiGlobin) are gene therapies with little clinical trial experience. Each faces a number of clinical, regulatory, and commercial hurdles prior to becoming successful.

Addendum

Stocks Mentioned In Important Disclosures

Ticker	Company Name
BLUE	bluebird bio

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Cowen and Company, LLC. New York (646) 562-1000 **Boston** (617) 946-3700 **San Francisco** (415) 646-7200 **Chicago** (312) 577-2240 **Cleveland** (440) 331-3531 **Atlanta** (866) 544-7009 **London** (affiliate) 44-207-071-7500

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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

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

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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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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 03/31/14

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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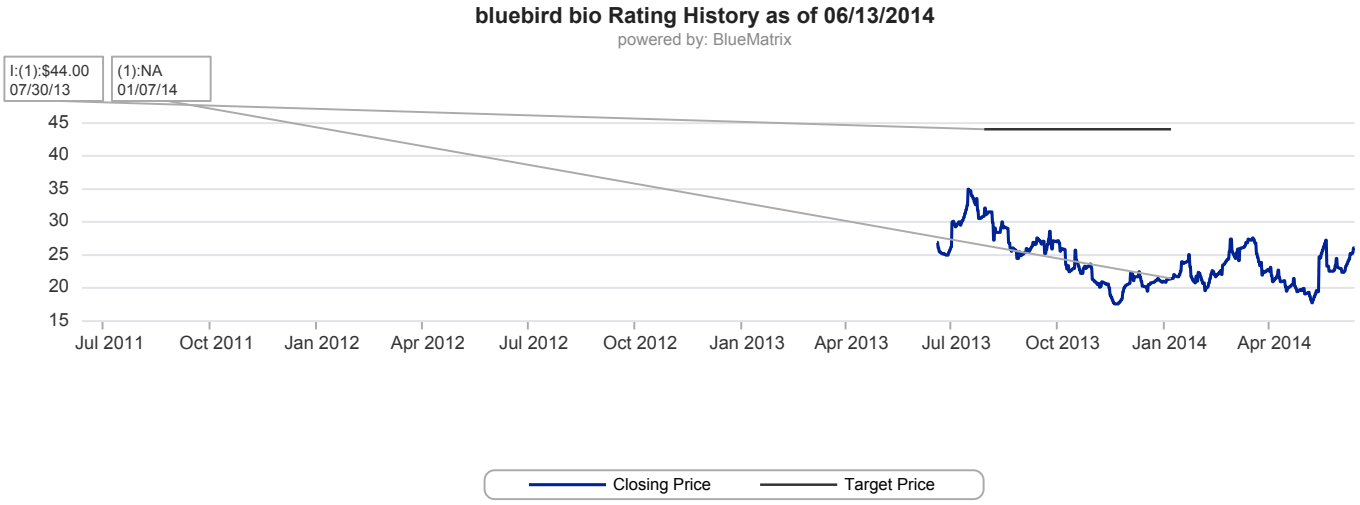

Legend for Price Chart:

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

Points Of Contact

Reaching Cowen

Main U.S. Locations

New York
599 Lexington Avenue
New York, NY 10022
646.562.1000
800.221.5616

Boston
Two International Place
Boston, MA 02110
617.946.3700
800.343.7068

Cleveland
20006 Detroit Road
Suite 100
Rocky River, OH 44116
440.331.3531

San Francisco
555 California Street, 5th Floor
San Francisco, CA 94104
415.646.7200
800.858.9316

Atlanta
3399 Peachtree Road NE
Suite 417
Atlanta, GA 30326
866.544.7009

Chicago
181 West Madison Street
Suite 1925
Chicago, IL 60602
312.577.2240

Houston
600 Travis Street
Suite 1970
Houston, TX 77002
281.657.6800

International Locations

Cowen International Limited

London
1 Snowden Street - 11th Floor
London EC2A 2DQ
United Kingdom
44.20.7071.7500

Cowen and Company (Asia) Limited

Hong Kong
Suite 1401 Henley Building
No. 5 Queens Road Central
Central, Hong Kong
852 3752 2333

@CowenResearch

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