Avalanche Biotechnologies

Equity Research

Company Quick Take

October 20, 2014

Price: $30.21 (10/17/2014)

Price Target: $45.00

OUTPERFORM (1)

Phil Nadeau, Ph.D.
646.562.1336
phil.nadeau@cowen.com

Cristina Ghenoiu, Ph.D.
646.562.1401
cristina.ghenoiu@cowen.com

Key Data

Symbol	NASDAQ: AAVL
Market Cap (MM)	$672.4

Highlights From Avalanche's Analyst Meeting At AAO

The Cowen Insight

On Saturday Avalanche held an analyst meeting at AAO. A physician panel discussion addressed some of the more prominent questions about AAVL's AVA-101 and increased our confidence in the competitive position of AVA-101. We continue to think that if AVA-101 is successfully developed it will have $1B+ market potential, and we recommend investors build a position in Avalanche.

Prominent Physicians Discuss AVA-101 And Gene Therapy At Avalanche's Analyst Meeting

On Saturday morning Avalanche held an analyst event at the annual meeting of the American Academy of Ophthalmology (AAO) in Chicago. Avalanche's analyst meeting featured a panel of wet AMD experts who discussed gene therapy as a treatment for wet AMD. Panel participants were Jeffrey Heier (Tufts), Szilard Kiss (N.Y. Presbyterian) Srinivus Sadda (UCLA) as well as Avalanche's Sam Barone and Roman Rubio. The panel addressed many of the most prominent questions about wet AMD gene therapy generally, and Avalanche's program specifically. We came away more confident that AVA-101 has a good chance of being successfully developed, and of capturing meaningful share of the $10B market for VEGF inhibitors in wet AMD. Highlights from the panel discussion follow.

Next Steps For Genzyme's Wet AMD Gene Therapy Program Unclear

Dr. Heier reviewed a presentation he gave earlier at AAO on the data generated thus far by the Genzyme and Avalanche gene therapy programs. As both deliver anti-VEGF gene therapy for wet AMD using an AAV vector, Genzyme's program is viewed by most investors as Avalanche's closest competitor. Dr. Heier made a couple of points which, to us, raise questions about the viability and competitiveness of the Genzyme program. In employing delivery by an intraviteal injection, instead of the subretinal injection used by Avalanche, Genzyme has seemingly sacrificed consistency of response for convenience. Dr. Heier noted that in its recently- completed Phase II trial, Genzyme made an assessment of whether a patients' wet AMD was likely to respond to anti-VEGF therapy. Genzyme characterized 11 patients in the trial as having AMD that should respond to anti-VEGF therapy. Of those 11, only 4 had a response to Genzyme's gene therapy, a 36% response rate. Dr. Heier noted that, in his opinion, consistency of response is a very important attribute of a gene therapy preparation, and that in order for a gene therapy to be viable, it needs to produce a response in more than 50% of VEGF-responsive patients, and perhaps as many as 75%. In its initial Phase 2 trial the Genzyme program did not achieve this bar, while in its Phase 2a Avalanche's AVA-101 did, as AVA-101 improved visual acuity in 5 of 6 patients (83% response rate). Genzyme has yet to announce plans for new or subsequent trials of its gene therapy, and Dr. Heier noted that discussions are ongoing about what to do next.

Subretinal Injections Require Precision, But Are A Skill That Can Be Mastered By Most Vitreoretinal Surgeons

As noted above, Avalanche's AVA-101 is delivered via a subretinal injection. Based on the available data, subretinal injections of AAV gene therapy appear to result in more consistent gene expression. Nonetheless, they are less convenient and more complicated than an intravitreal injection, and so many investors question whether AVA-101's subretinal injection could result in more adverse events in clinical trials, or limit AVA-101's market opportunity. This was a topic touched on at Cowen's Therapeutics conference this month, and the panel at Avalanche's analyst meeting discussed it extensively. Avalanche's panel noted that the procedure requires approximately 20 minutes in the operating room. Although it is a procedure which requires skill and precision, the panel thinks that it is a technique that can be mastered with some training by most vitreoretinal surgeons. The panel noted that in Avalanche's future clinical trials there will need to be standardized training procedures which should include at least a day of formal teaching, and a day of evaluation in the wet lab to ensure that investigators are sufficiently proficient. Avalanche's panel thinks such an amount of preparation will be adequate to ensure that adverse event rates due to the procedure will be low. Many vitreoretinal surgeons deliver TPA subretinally for sub macular hemorrhages and the panel noted that the procedure is typically associated with a less than 2% rate of adverse events. Avalanche's panel said that if AVA-101's duration of activity is over a year, its subretinal delivery will be accepted by physicians.

It Is Unclear If Geographic Atrophy Is A Consequence Of The Disease Process or VEGF Therapy Itself, But It Is Clear That Under-Treatment With Anti-VEGFs Results In Vision Loss

Some worry that treatment of wet AMD with anti-VEGFs worsens geographic atrophy, and therefore that continual VEGF inhibition over a long time by gene therapy could accelerate atrophy even more. Saturday's panel debated the relationship between geographic atrophy and anti-VEGF therapy. Some of the physicians on the panel think that VEGF therapy does worsen geographic atrophy, and others take the position that geographic atrophy is unrelated to VEGF therapy and is simply a consequence of the underlying disease process. Nonetheless, Avalanche's panel unanimously agreed that the most prominent reason for vision loss in wet AMD today is inadequate treatment with anti-VEGF therapy, and that the under-treatment is often due to the requirement for frequent injections, and the logistical issues associated with frequent and regular visits to the physician necessitated by the current anti-VEGF therapies. Therefore, Avalanche's panel is hopeful that if gene therapy is able to greatly reduce the number of injections and physician visits required, patients' vision will be much better preserved. The panel asserted that the likelihood of better patient management with gene therapy is well worth the theoretical risk of possibly more geographic atrophy.

If Successfully Developed, AVA-101 Will Be Used To Treat Patients Who Need Consistent VEGF Injections, Which Is The Vast Majority Of The Market

The physicians are hopeful that AVA-101 will control patients' wet AMD for years after a single injection. They note that some patients can be adequately treated by 1 or 2 VEGF injections, but that the majority of patients require frequent therapy. They estimate that only approximately 5-10% of their anti-VEGF injections are in naive eyes, implying that >90% of anti-VEGF revenue in wet AMD comes from patients who

need regular injections. It is these patients who could benefit most from a therapy like AVA-101. Should AVA-101 make it to market, the physicians suggest that they would probably give patients 1 or 2 anti-VEGF injections upon their initial wet AMD diagnosis. If those injections do not halt their disease and subsequent anti-VEGF therapy is necessary, the physicians would seriously consider AVA-101.

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

The majority of Avalanche's market capitalization is dependent upon the success of lead candidate AVA-101. AVA-101's value could be adversely impacted should its clinical trials fail, should the regulatory agencies deny approval, or should its commercial opportunity not materialize as we project. In fact, all of Avalanche's drug candidates face clinical and regulatory risk. With the future development path depending on the evolution of clinical data, revenue forecasts are uncertain. The commercial outlook for Avalanche's 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 Avalanche's projected market exclusivity depends on patents, which are subject to challenge by potential competitors.

Addendum

Stocks Mentioned In Important Disclosures

Ticker	Company Name
AAVL	Avalanche Biotechnologies

Analyst Certification

Each author of this research report hereby certifies that (i) the views expressed in the research report accurately reflect his or her personal views about any and all of the subject securities or issuers, and (ii) no part of his or her compensation was, is, or will be related, directly or indirectly, to the specific recommendations or views expressed in this report.

Important Disclosures

Cowen and Company, LLC and or its affiliates make a market in the stock of Avalanche Biotechnologies securities.

Avalanche Biotechnologies has been client(s) of Cowen and Company, LLC in the past 12 months.

Cowen and Company, LLC and/or its affiliates expect to receive, or intend to seek, compensation for investment banking services in the next 3 months from Avalanche Biotechnologies.

Avalanche Biotechnologies is or was in the past 12 months a client of Cowen and Company, LLC; during the past 12 months, Cowen and Company, LLC provided IB services.

Cowen and Company, LLC and/or its affiliates received in the past 12 months compensation for investment banking services from Avalanche Biotechnologies.

Cowen and Company, LLC and/or its affiliates managed or co-managed a public offering of Avalanche Biotechnologies within the past twelve months.

Cowen and Company, LLC compensates research analysts for activities and services intended to benefit the firm's investor clients. Individual compensation determinations for research analysts, including the author(s) of this report, are based on a variety of factors, including the overall profitability of the firm and the total revenue derived from all sources, including revenues from investment banking. Cowen and Company, LLC does not compensate research analysts based on specific investment banking transactions.

Disclaimer

This research is for our clients only. Our research is disseminated primarily electronically and, in some cases, in printed form. Research distributed electronically is available simultaneously to all Cowen and Company, LLC clients. All published research can be obtained on the Firm's client website, https://cowenlibrary.bluematrix.com/client/library.jsp.

Further information on any of the above securities may be obtained from our offices. This report is published solely for information purposes, and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state where such an offer or solicitation would be illegal. Other than disclosures relating to Cowen and Company, LLC, the information herein is based on sources we believe to be reliable but is not guaranteed by us and does not purport to be a complete statement or summary of the available data. Any opinions expressed herein are statements of our judgment on this date and are subject to change without notice.

For important disclosures regarding the companies that are the subject of this research report, please contact Compliance Department, Cowen and Company, LLC, 599 Lexington Avenue, 20th Floor, New York, NY 10022. In addition, the same important disclosures, with the exception of the valuation methods and risks, are available on the Firm's disclosure website at https://cowen.bluematrix.com/sellside/Disclosures.action.

Price Targets: Cowen and Company, LLC assigns price targets on all covered companies unless noted otherwise. The price target for an issuer's stock represents the value that the analyst reasonably expects the stock to reach over a performance period of twelve months. The price targets in this report should be considered in the context of all prior published Cowen and Company, LLC research reports (including the disclosures in any such report or on the Firm's disclosure website), which may or may not include price targets, as well as developments relating to the issuer, its industry and the financial markets. For price target valuation methodology and risks associated with the achievement of any given price target, please see the analyst's research report publishing such targets.

Notice to UK Investors: This publication is produced by Cowen and Company, LLC which is regulated in the United States by FINRA. It is to be communicated only to persons of a kind described in Articles 19 and 49 of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005. It must not be further transmitted to any other person without our consent.

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

COWEN AND COMPANY RATING DEFINITIONS

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

Sell – The fundamentals/valuations of the subject company are deteriorating and the investment return is expected to be 5 to 15 percentage points lower than the general market return

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

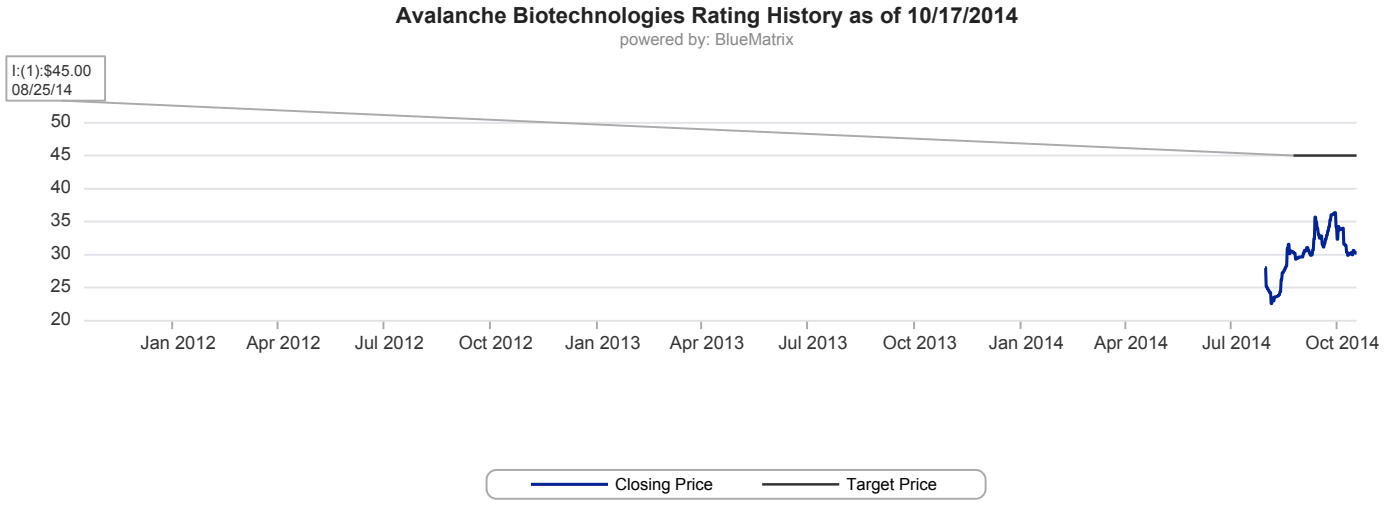
Cowen And Company Rating Definitions

Distribution of Ratings/Investment Banking Services (IB) as of 09/30/14

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	440	59.95%	105	23.86%
Hold (b)	278	37.87%	10	3.60%
Sell (c)	16	2.18%	0	0.00%

(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.

Note: "Buy", "Hold" and "Sell" are not terms that Cowen and Company, LLC uses in its ratings system and should not be construed as investment options. Rather, these ratings terms are used illustratively to comply with FINRA and NYSE regulations.



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

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

Cowen and Company