Avalanche Biotechnologies (AAVL)

SunTrust Robinson Humphrey

Await Further AVA-101 Clarity, Lack of Near-Term Catalysts, DGrading to Neutral

Downgrading to Neutral, Reducing PT to $25 from $60

What's Incremental
Phase IIa data for AAVL's AVA-101 in wet AMD appear somewhat positive: 42.9% of pts improved/maintained stable vision with =<2 Lucentis injections (vs 9.1% control). Yet, is visual acuity (VA) improvement with AVA-101 vs. control (+2.2 vs -9.3 letters) due to insufficient Lucentis injections of control pts (median of 4) and/or the "over-treatment" of AVA-101 pts (median of 2). OCT increase can be explained by baseline imbalances, but we await clarity on the curves. We anticipate AAVL may trade sideways on lack of near-term catalysts (REGN opt-in could be a risk) and thus downgrade to Neutral.

Topline Phase IIa results paint an incomplete picture of AVA-101's preliminary profile. AAVL announced results from the Phase IIa study (single center, Lion's Eye Institute, Australia) in wet AMD. Over 52 weeks, the 21 patients given AVA-101 required a median of 2 Lucentis rescue injections, compared to 4 injections for the 11 control patients. Overall visual acuity (BCVA) increased by 2.2 letters in the AVA-101 arm vs. a decrease of 9.3 letters in the control arm, for a 11.5 letter difference. Stable BCVA was defined as >-5 letter change. 42.9% patients improved or maintained stable BCVA, with 2 or fewer injections. 23.8% of all patients saw a BCVA improvement of 10 or more letters with 2 or fewer injections. We spoke with management, who explained that an imbalance in retinal thickness was observed at baseline between the 2 study arms (control patients had higher retinal thickness and thus, more room to improve). Therefore, although the 52-week mean change from baseline in retinal thickness was +25 um for AVA-101 treated patients compared to a decrease of -56 um for control, this delta occurred in the first 8 weeks and the difference in OCT between the 2 arms remained constant post this period.

While we view these data as positive for AVA-101, multiple questions remain given the presentation of these results. Questions we would have liked answered are: 1) what was the overall % of patients who experienced stable or improved BCVA versus decline?, 2) was the BCVA improvement with AVA-101 driven by patients getting more than 2 Lucentis injections? 3) what was the impact on mean BCVA/median injection numbers of the treatment naive patients (1 in the AVA-101 and 2 in the control arm)? and 4) were the control patients under-treated with Lucentis? Management explained that Phase IIa patients (although milder than Phase I participants), harbored rather severe wet AMD (with baseline fibrosis and pigment epithelium detachment) and were administered an adequate number of injections. **Net net, it is unclear to us based on the disclosed topline**

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SEE PAGE 5 FOR REQUIRED DISCLOSURE INFORMATION

↓ Buy to Neutral

Price Target: $25.00
Prior: $60.00

Price (Jun. 15, 2015)	$38.88
52-Wk Range	$60.08-$22.60
Market Cap ($M)	$980
ADTV	355,859
Shares Out (M)	25.2
Short Interest Ratio/% Of Float	10.0%
TR to Target	(35.7)%

Cash Per Share	$8.02
Cash And Equivalents ($M)	$290.1

	2014A	2015E		2016E	
		Curr.	Prior	Curr.	Prior
EPS Adjusted					
1Q	($0.45)	($0.38)A	($0.38)	--	
2Q	($2.27)	($0.50)	($0.50)	--	
3Q	($0.50)	($0.62)	($0.62)	--	
4Q	($0.46)	($0.71)	($0.71)	--	
FY	($2.46)	($2.21)	($2.21)	($3.10)	($3.10)
P/E	NM	NM		NM	
Consensus EPS Adjusted					
FY	($2.61)	($1.82)	($1.82)	($2.28)	($2.28)
Revenue ($M)					
FY	$1	$1	$1	$0	$0
P/Sales	979.8x	979.8x		--	
Consensus Rev					
FY	$1	$0	$0	$0	$0

FYE Dec
Quarterly values may not add to the annual value due to rounding.

data if the impressive BCVA letter difference between the arms was due to control patients not being given sufficient rescue Lucentis injections or due to active patients being "over-rescued" (i.e. given too many Lucentis injections). A key question is physician preference for a therapy yielding BCVA improvement with more injections, versus one aimed at maintaining stable BCVA with fewer injections. For clarity on AVA-101's profile, full Phase IIa results are likely to be presented in H2/15 at either ASRS (July 13-14, Vienna, Austria), Retina Society meeting (Oct 7-11, Paris, France) or AAO (Nov 14-17, Las Vegas). We also expect 2-year data in H1/mid-16 - however, the control arm may be difficult to follow. We anticipate investors will be looking towards full Phase IIb results disclosure (given first patient in by YE15, likely not before early 2017).

Long-term follow up from Phase I looks good, but data are incomplete. Also disclosed today were long-term, 36-month follow up results from the Phase I trial of AVA-101. These data are encouraging, with a mean BCVA change from baseline of +0.5 letters and an average of 0.71 rescue injections per year. However, results from control patients were not disclosed, rendering it difficult to assess the durability of AVA-101. We look towards 18 and 36 month analyses of Phase IIa data for additional color on persistence.

With questions remaining after Phase IIa and few upcoming catalysts, we are downgrading to Neutral. While we view the Phase IIa data as positive for informing AAVL's Phase IIb trial, questions remain - we look towards some clarity at a conference presentation in H2/15 and 2 year data in H1/16 or mid-16. In addition, we anticipate limited positive impact from other catalysts through mid-16 (color on the Phase IIb design and launch by YE15, earlier stage program entering the clinic). REGN has a right of first negotiation to opt into the development of AVA-101 post this data (though it could choose to wait given outstanding questions with the Phase IIa data). Should REGN not opt in at this point, it will have to re-negociate this right around Phase IIb results. We are downgrading AAVL to Neutral from Buy and reducing our price target to $25. We are lowering out probability of success for the AVA-101 program to 20% in the US (from 55%) and 12% in the EU (from 20%) and raising our discount rate from 12% to 13%.

Figure 1: Upcoming Expected Milestones

Product	Timing	Indication	Event
AVA-101	Mid-2015	Wet age-related macular degeneration	Potential Regeneron opt-in
AVA-101	July 13-14	Wet age-related macular degeneration	Potential Phase IIa update at ASRS
AVA-101	H2 2015	Wet age-related macular degeneration	U.S. IND Filing
AVA-101	Oct 7-11	Wet age-related macular degeneration	Potential Phase IIa update at AAO
AVA-101	Nov 14-17	Wet age-related macular degeneration	Potential Phase Iia update at Retina Society meeting
AVA-101	2015	Wet age-related macular degeneration	Publication of 52-week Phase I data in a medical journal
AVA-201	2015	Prevention of wet AMD	Completion of preclinical work for IND filing
AVA-322/AVA-323	H2 2016	Color Blindness	U.S. IND Filing

Source: STRH analysis and Company reports

Avalanche Biotechnologies

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Consolidated Income Statement

($thousands, except per share data)	FY 2014A	Mar Q1 2015A	Jun Q2 2015E	Sep Q3 2015E	Dec Q4 2015E	FY 2015E	FY 2016E	FY 2017E	FY 2018E	FY 2019E	FY 2020E
Revenue											
AVA-101	$ -	-	-	-	-	$ -	$ -	$ -	$ -	$ -	$ 128,387
Total product revenue						$ -	$ -	$ -	$ -	$ -	$ 128,387
Collaboration and license revenue	**572**	203	203	203	203	**812**	**812**	**812**	**812**	**812**	**812**
Total Revenue	**$ 572**	**$ 203**	**$ 203**	**$ 203**	**$ 203**	**$ 812**	**$ 812**	**$ 812**	**$ 812**	**$ 812**	**$ 129,199**
COGS	-	-	-	-	-	-	-	-	-	-	6,419
Gross profit	572	203	203	203	203	812	812	812	812	812	122,779
Operating expense											
R&D (GAAP)	16,976	5,621	7,978	10,121	11,901	35,621	72,221	98,041	118,334	132,711	143,560
SG&A (GAAP)	7,998	4,143	4,744	5,711	6,302	20,900	25,556	34,210	42,502	65,114	87,001
Stock-based compensation	8,564	-	-	-	-	-	-	-	-	-	-
Total operating expense	24,974	9,764	12,722	15,832	18,203	56,521	97,777	132,251	160,836	197,825	230,561
Operating income (loss)	**(24,402)**	**(9,561)**	**(12,519)**	**(15,629)**	**(18,000)**	**(55,709)**	**(96,965)**	**(131,439)**	**(160,024)**	**(197,013)**	**(107,782)**
Interest Income (expense), net	(6)	52	65	62	58	238	127	173	134	130	122
Other income (expense), net	(70)	-	-	-	-	-	-	-	-	-	-
Change in fair value of warrant liabilities	(722)										
Total Other Income	(1,002)	52	65	62	58	238	127	173	134	130	122
Deemed dividend	(3,230)										
Income before income taxes	(25,404)	(9,509)	(12,454)	(15,567)	(17,942)	(55,471)	(96,838)	(131,266)	(159,890)	(196,883)	(107,659)
Provision for income taxes	-	-	-	-	-	-	-	-	-	-	-
Net gain (loss)	**(28,634)**	**(9,509)**	**(12,454)**	**(15,567)**	**(17,942)**	**(55,471)**	**(96,838)**	**(131,266)**	**(159,890)**	**(196,883)**	**(107,659)**
FX translation adjustment											
Net gain (loss) applicable to common shareholders	**$ (28,634)**	**$ (9,509)**	**$ (12,454)**	**$ (15,567)**	**$ (17,942)**	**$ (55,471)**	**$ (96,838)**	**$ (131,266)**	**$ (159,890)**	**$ (196,883)**	**$ (107,659)**
GAAP EPS (diluted)	**$ (2.46)**	**$ (0.38)**	**$ (0.50)**	**$ (0.62)**	**$ (0.71)**	**$ (2.21)**	**$ (3.10)**	**$ (4.16)**	**$ (4.83)**	**$ (5.28)**	**$ (2.75)**
Weighted shares outstanding basic and diluted (k)	11,651	24,887	25,011	25,136	25,262	25,074	31,229	31,541	33,118	37,274	39,138
Margin Analysis:											
Cost of product sales	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	5%	5%
Product gross margin	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	95%	95%
R&D (GAAP)	2968%	2769%	3930%	4986%	5863%	4387%	8894%	12074%	14573%	16344%	111%
SG&A (GAAP)	1398%	2041%	2337%	2813%	3104%	2574%	3147%	4213%	5234%	8019%	67%
Stock-based compensation expense	1497%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Total operating expense	4366%	4810%	6267%	7799%	8967%	6961%	12042%	16287%	19807%	24363%	178%
Operating margin	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-19707%	-24263%	-83%
Income tax provision	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Net margin (GAAP)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-19691%	-24247%	-83%
Y/Y change:											
Total revenue	119%	677%	150%	100%	100%	142%	100%	100%	100%	100%	15911%
AVA-101 revenue	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
R&D (GAAP)	689%	518%	158%	76%	65%	110%	103%	36%	21%	12%	8%
SG&A (GAAP)	349%	471%	218%	138%	86%	161%	22%	34%	24%	53%	34%
Stock-based compensation expense	N/A	0%	0%	0%	0%	0%	N/A	N/A	N/A	N/A	N/A
Total operating expense	535%	497%	177%	94%	72%	126%	73%	35%	22%	23%	17%
Operating income	606%	495%	181%	97%	73%	128%	74%	36%	22%	23%	-45%
Net income (GAAP)	440%	472%	50%	88%	73%	94%	75%	36%	22%	23%	-45%
GAAP EPS (diluted)	70%	-16%	-78%	23%	54%	10%	-40%	-34%	-16%	-9%	48%
Shares outstanding - GAAP	217%	578%	581%	53%	12%	115%	25%	1%	5%	13%	5%

Source: STRH Research, Company Reports

Company Description

Avalanche Biotechnologies, Inc. is a clinical-stage biotechnology company that develops novel gene therapies to treat patients with sight-threatening ophthalmic diseases. Its products are used for the treatment of wet age-related macular degeneration and Juvenile X-linked Retinoschisis by inducing a sustained expression of a therapeutic protein with a one-time administration in the eye. The company was founded by Mark S. Blumenkranz, Thomas W. Chalberg and Steven D. Schwartz on July 17, 2006 and is headquartered in Menlo Park, CA.

Investment Thesis

Avalanche is one of the slew of new entrants in the biotech space, focused on gene therapy. Broad investor interest in the renaissance of gene therapy is evidenced by the strong performance of most of these stocks over their S1 price. This product consists of an adeno-associated vector-based gene therapy, with the potential to disrupt and expand the $6B+ anti-VEGF market. Clinical results generated to date are suggestive of activity in a small number of patients with advanced disease. A randomized Phase IIa single center study is ongoing in Australia yielded somewat positive results, but questions remain. Given AVA-101's mechanism of action similar to anti-vascular endothelial growth factor (VEGF) biologics Lucentis and Eylea, the product could also have utility beyond wet AMD, in diseases such as retinal vein occlusion or diabetic macular edema (where Lucentis and Eylea are the standard of care). A follow-on preclinical gene therapy product AVA-201 is expected to undergo IND-enabling studies in 2015 for the prevention of high risk wet AMD. Avalanche is collaborating with Regeneron for the development of novel gene therapies for eye diseases, with the first product (preclinical stages) AVA-311 to address the orphan disease X-linked retinoschisis (XLRS). Notably, Regeneron also retains a time-limited right to first negotiation of rights to AVA-101.

Valuation and Risks

Valuation

We arrive at our price target of $25 by means of a sum-of-the-parts discounted cash flow analysis, which ascribes $11.28/share to AVA-101 U.S. sales, $3.11 to AVA-101 E.U. sales, and $8.04/share to cash. We assign AVA-101 in a probability of success of 20% in the U.S. and 12% in the E.U. We assume a discount rate of 13% and a 1% terminal growth rate. We do not model for any additional indications for AVA-101 beyond wet AMD. We do not include any value for AVA-201, AVA-311, or any other follow on products in our valuation.

Investment risks

The primary downside investment risks for Avalanche include the following:

• **Clinical and safety risk**: Phase I results presented to date showcased some intriguing signs of activity for Avalanche's AVA-101. The limitations of these data, however, include the small number of patients, a single center whereby doctors were well familiar with subretinal injection, and participants with advanced wet AMD who experienced tremendous increases in best corrected visual acuity. There remains the risk that Phase IIa and Phase IIb data do not recapitulate earlier findings due to differences in patient baseline characteristics, variability in time of assessment and determination of whether an anti-VEGF injection is needed, variability in efficacy measurements. There also remains a risk (albeit minimal) that in vivo dosing of AVA-101 could lead to an exaggerated immune reaction, resulting in loss of anti-VEGF molecule expression of significant loss of eye tissue.
• **Regulatory risk:** No gene therapy product has been approved in the U.S. to date, and in spite of the FDA's guidance there remain questions about the appropriate study design for pivotal gene therapy trials, especially for orphan diseases. The agency may require additional information on manufacturing methodology, as well as facilities where all the moving parts of a complex therapy are generated.
• **Commercial risk:** Given the novelty of gene therapy, there remains a risk that physicians are reluctant to prescribe AVA-101 to their patients. We note the risk of AVA-101 not reaching our sales estimates due to potential pricing and reimbursement issues, lower than expected penetration, or lack of ability to effectively target the broad wet AMD market.
• **Competitive Risk:** AVA-101 is entering the established wet AMD market, where two branded products (RHHBY's Lucentis and REGN's Eylea) and off-label Avastin are competing for share of the prevalent patient pool. Furthermore, AVA-101 competes with products such as Ophthotech's Fovista and Allergan's DARPins, which offer alternatives to the current anti-VEGF standard of care. Beyond

monthly or every other month injections, AVA-101 is also competing with other gene therapies. There is a risk that AVA-101 would not capture significant share of the wet AMD market, or of the retinal vein occlusion or diabetic macular edema markets.
• **Financial and partnership risk:** Avalanche does not currently recognize any revenue related to product sales. Given the expenses associated with clinical drug development, we forecast that the company could issue additional equity to finance its activities. There remains a risk that the company's cash reserves may be significantly depleted while attempting to fulfill collaborative obligations for partner Regeneron. There is a risk that no appropriate candidates emerge from the collaboration with Regeneron, thereby jeopardizing the non-dilutive cash inflow associated with this partnership (we do not model for any revenue associated with the partnership apart from the $6.5M upfront payment).

Upside investments risks include:
• **Partnership risk:** Avalanche's collaborator REGN has the right to first negotiation to AVA-101 (timed) and could opt in to develop the product, likely putting upward pressure to AAVL shares.

Companies Mentioned in This Note

Regeneron Pharmaceuticals (REGN, $499, NR)

Analyst Certification

I, Salveen Richter , hereby certify that the views expressed in this research report accurately reflect my personal views about the subject company(ies) and its (their) securities. I also certify that I have not been, am not, and will not be receiving direct or indirect compensation in exchange for expressing the specific recommendation(s) in this report.

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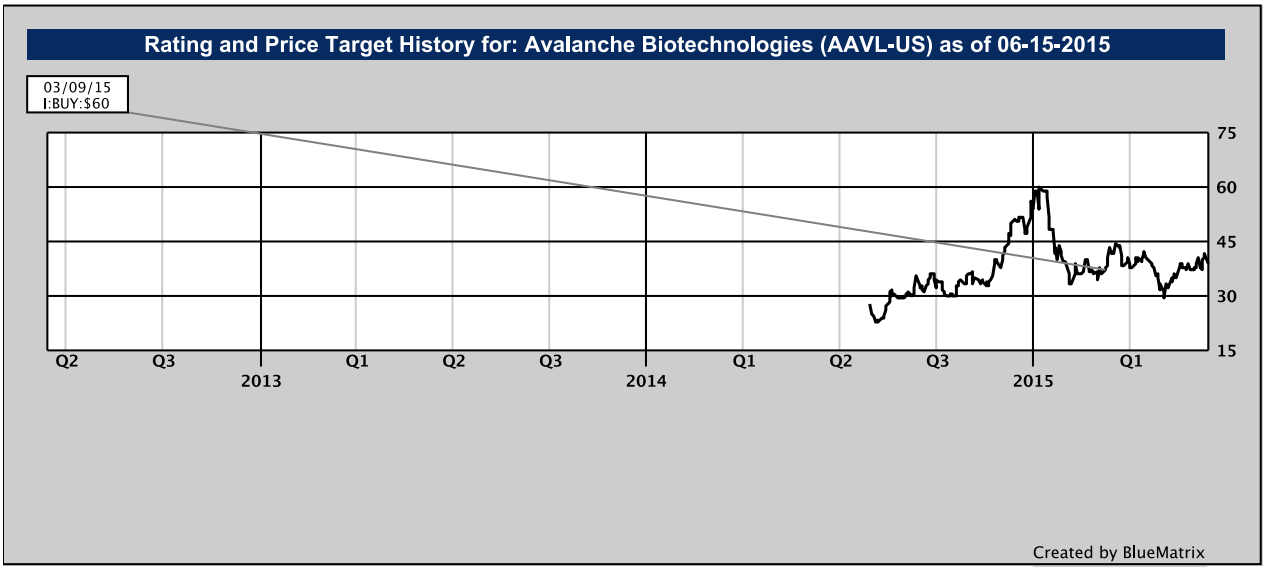

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