Avalanche Biotechnologies (AAVL)

On the Lookout for a Favorable AVA-101 Phase IIa Outcome

Buy

Price Target: $60.00
Prior: $60.00

Price (Jun. 4, 2015)	$38.82
52-Wk Range	$60.08-$22.60
Market Cap ($M)	$978
ADTV	322,699
Shares Out (M)	25.2
Short Interest Ratio/% Of Float	10.6%
TR to Target	54.6%

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	978.3x	978.3x		--	
Consensus Rev					
FY	$1	$0	$0	$0	$0

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

What's Incremental

AAVL's key upcoming catalyst is the readout of the AVA-101 Phase IIa study in wet AMD (in conjunction with the 36-month Phase I update, with visibility into durability) in June/July. We believe AVA-101 is well positioned to show activity on the key metric - reduction in the no. of Lucentis injections vs. control - while maintaining stable visual acuity and retinal thickness (any letter gain a nice upside). While REGN has a timed first right of negotiation to co-develop AVA-101, AAVL may chose to retain the program. We believe AAVL shares could see a significant uptick on a positive scenario.

Looking towards an inflection point for AAVL with the readout of AVA-101 Phase IIa results in June/July. The major upcoming AAVL catalyst is the readout of the Phase IIa study of lead gene therapy product, AVA-101, in wet age-related macular degeneration, an eye disorder. This is a safety study (not powered for efficacy), but we believe AVA-101 is well positioned to enable reduction in the number of Lucentis injections (key efficacy measure), based on positive readthrough from 12-month Phase I data (albeit the Phase II population is milder), with 10x fewer injections/year achieved with AVA-101 versus control. Lucentis rescue injections were given with signs of disease worsening (decrease in visual acuity - BCVA no. of letters, and increase in retinal thickness - OCT), though the exact cutoff for these criteria has not been disclosed. We spoke with management, and an effective therapy could result in either 1) potential for fewer injections with maintenance of stable BCVA and OCT or 2) patient over-rescue (through Lucentis injections) with BCVA letter gains. **Per historical trials, we anticipate patients in the control arm to require 3-6 Lucentis injections to maintain stable BCVA and OCT and look toward fewer injections in the AVA-101 arm (KOLs believe a total of 0-2/year would be meaningful, or a significant % reduction).**

We assign a 75% probability to positive scenarios: A positive scenario entails fewer (potentially total of 0-2 or a significant % reduction) Lucentis injections with AVA-101 vs. control, stable BCVA (or a positive no.) and stable OCT (or a reduction), (rather than the impressive BCVA improvement seen in Phase I given the milder wet AMD population), **with potentially up to 50-100%+ gains in AAVL shares, dependent on the magnitude of the clinical benefit** (best case scenario - 0 Lucentis injections with AVA-101, OCT decrease and >1+ BCVA letter gain). Negative scenarios would entail no difference in Lucentis injection numbers and/or a significant BCVA letter loss, OCT gain (shares trading towards cash of $8/share on worse case scenario, <5% probability). While REGN has the right of first negotiation to co-develop AVA-101, AAVL may chose to develop the product independently. We model for peak AVA-101 U.S./E.U. sales of $2B+ in 2026.

Salveen Richter, CFA
212-319-3728
salveen.richter@suntrust.com

Raluca Pancratov, Ph.D.
212-303-4178
raluca.pancratov@suntrust.com

SEE PAGE 5 FOR REQUIRED DISCLOSURE INFORMATION

We believe AVA-101 is well positioned to yield at least stable visual acuity in the Phase IIa study. Per published data, dramatic BCVA increase (increase in number of letters) is generally seen in 1) treatment naive wet AMD patients starting anti-VEGF therapy (e.g. pivotal trials of Eylea, Lucentis), or 2) patients poorly controlled with anti-VEGF, switching therapy (e.g. from Lucentis to Eylea). A key difference between the Phase I and IIa studies of AVA-101 were the baseline patient characteristics (median BCVA of 36.5 letters, OCT of 549 microns in Phase I), with milder wet AMD patients (N=32) tested in the Phase IIa (median BCVA of 63 and OCT of 332.5). The 6 AVA-101 treated Phase I patients achieved impressive +8.7 (n=3) and +6.3 (n=3) BCVA letter improvement (high and low dose) vs. control at -3.5 (N=2) at month 12. However, Phase IIa patient demographics are suggestive of a milder population, better controlled with anti-VEGF injections. We anticipate Phase IIa patients (largely treatment-experienced) are likely to maintain stable BCVA and OCT, in line with year 2 data seen in large, pivotal trials for anti-VEGF agents (CATT, HARBOR), while BCVA and OCT improvement is upside to our estimates. A loss of ~3-5 letters is clinically indicative of stable vision; however, we believe such an event would be viewed as negative by the Street, causing AAVL share weakness (however, this needs to be evaluated in the context of reduction in Lucentis injections versus control arm).

36-month Phase I results slated to provide important durability trends. AAVL guided that topline 36-month updated Phase I results will be announced at the same time as Phase IIa results. A presentation at a medical meeting would follow in H2/15. The primary readout of the data is safety, but key investor questions concerning durability may also be addressed. Post the 12-month study completion, BCVA and OCT data were collected at 18 and 36 months, with patient-reported historical information (including number of anti-VEGF injections) collected at each visit. Although these data will be approached cautiously, we look towards continued benefit with AVA-101, with respect to fewer annual rescue Lucentis injections, and stable visual acuity.

AAVL Upcoming Milestones

Product	Timing	Indication	Event
AVA-101	**Mid-2015**	**Wet age-related macular degeneration**	**Readout of a Phase IIa study**
AVA-101	H2 2015	Wet age-related macular degeneration	U.S. IND Filing
AVA-101	**Mid-2015**	**Wet age-related macular degeneration**	**36-month data from the Phase I study (topline)**
AVA-101	Mid-2015	Wet age-related macular degeneration	Potential Regeneron opt-in
AVA-101	**H2 2015**	**Wet age-related macular degeneration**	**Conference presentation of 36-month Phase I data**
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: Company filings and STRH analysis

SUNTRUST ROBINSON HUMPHREY

Avalanche Biotechnologies

(NASDAQ: AAVL)

Salveen Richter, CFA
(212) 319-3728
salveen.richter@suntrust.com

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. Furthermore, AAVL shares are currently down off its highs at the end of December, providing an entry point ahead of readout of the Phase IIa study of lead product AVA-101 for wet age-related macular degeneration (AMD) in mid-2015. 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, with results expected, as noted, mid-2015. 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 $60 by means of a sum-of-the-parts discounted cash flow analysis, which ascribes $46.24/share to AVA-101 U.S. sales, $6.11 to AVA-101 E.U. sales, and $8.04/share to cash. We assign AVA-101 in a probability of success of 55% in the U.S. and 25% in the E.U. We assume a discount rate of 12% 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 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).

Companies Mentioned in This Note

Regeneron Pharmaceuticals (REGN, $518.62, 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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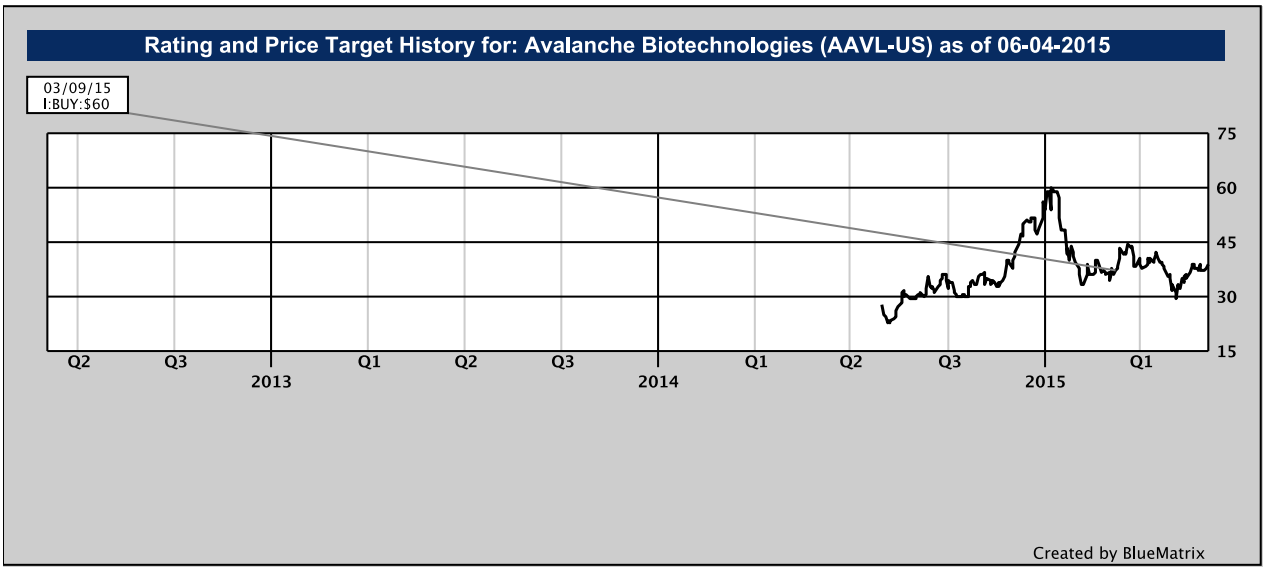

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*Total return (price appreciation + dividends)
**Price targets are within a 12-month period, unless otherwise noted
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Legend for Rating and Price Target History Charts:
D = drop coverage
I = initiate coverage
T = transfer coverage

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Coverage Universe			Investment Banking Clients Past 12 Months		
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Neutral	255	45.78%	Neutral	52	20.39%
Sell/Reduce	6	1.08%	Sell/Reduce	1	16.67%

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