

Avalanche Biotechnologies (AAVL)

Overweight

AAO Conference Update: Path Being Paved For Gene Therapy

CONCLUSION

The retina subspecialty days of the American Academy of Ophthalmology (AAO) annual meeting were held this past Friday and Saturday in Chicago. Although AAVL was not presenting any new data at the conference, the company hosted a KOL panel with retinal specialists involved in the gene therapy studies. In addition, an analysis on geographic atrophy (GA) from anti-VEGF treatment was also presented during the conference. We also saw multiple presentations highlighting potential concerns of the peak /trough PK profile of sustained, multi-year anti-VEGF therapy, which could benefit the smoother anti-VEGF profile of gene therapy. Reiterate OW and \$39 price target.

- **Subretinal vs intravitreal gene therapy:** The issue of subretinal injection vis-à-vis intravitreal injection was a topic of discussion both at the panel and at the conference. Although subretinal injection is not a routine procedure for the majority of retinal surgeons, it does not sound as though it will be a significant barrier to adoption as the skill is well within retinal specialists' skillset and similar to current procedures such as surgery for submacular hemorrhages. With the current vectors in the clinic, the subretinal approach provides higher protein expression levels, but AAVL (and AGTC) is currently working on developing new vectors that when injected intravitreally, can move through the ILM (inner limiting membrane) to efficiently transfect.
- **AGTC/GENZ review:** No new data were presented on the Genzyme / AGTC gene therapy trial for wet AMD. Results were presented previously, and were briefly summarized during the conference and discussed at the panel. One of the panel members was involved in the preclinical work and suggested that low Flt protein expression levels with intravitreal delivery explained the 4 responders out of a potential 11 in the clinical trial.
- **KOLs agree on the initial patient population:** Since there is a minority of patients who respond quickly to only 1 or 2 injections, KOLs on the panel agreed that the ideal candidates for gene therapy are patients who require several more injections after starting on currently available anti-VEGF therapy, i.e. those likely to become "treatment addicts". Our model reflects this assumption, as we currently model modest penetration into the incident patient population.
- **New data on geographic atrophy in wet-AMD:** Data from a post-hoc analysis of GA in the Lucentis HARBOR study was presented. The analysis indicated that the results roughly mirrored those seen in previous post-hoc analyses in large trials. During the panel, KOLs emphasized the importance of sustained treatment of wet-AMD, given the substantial efficacy significantly outweighs any theoretical risks.

RISKS TO ACHIEVEMENT OF PRICE TARGET

AAVL gene therapy candidates may fail to achieve target development steps.

COMPANY DESCRIPTION

AAVL is a pioneer in gene therapy, targeting ophthalmic indications.

YEAR	REVENUE (US\$ m)						EARNINGS PER SHARE (US\$)					
	Mar	Jun	Sep	Dec	FY	FY RM	Mar	Jun	Sep	Dec	FY	FY P/E
2013A	—	—	—	—	0.5	1,329.2x	—	—	—	—	(0.74)	NM
2014E	0.0A	0.1A	1.5	1.5	3.2	207.7x	(0.11)A	(0.28)A	(0.18)	(0.18)	(0.77)	NM
2015E	3.0	3.0	3.0	3.0	12.0	55.4x	(0.18)	(0.22)	(0.26)	(0.30)	(0.97)	NM

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Avalanche Biotechnologies, Inc.

PRICE: US\$30.21

TARGET: US\$39.00

DCF thru 2024, 11% discount rate, 5% terminal growth rate

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Changes	Previous	Current
Rating	—	Overweight
Price Tgt	—	US\$39.00
FY14E Rev (mil)	—	US\$3.2
FY15E Rev (mil)	—	US\$12.0
FY14E EPS	—	US\$(0.77)
FY15E EPS	—	US\$(0.97)
52-Week High / Low	US\$36.78 / US\$22.00	
Shares Out (mil)	22.0	
Market Cap. (mil)	US\$664.6	
Avg Daily Vol (ooo)		
Net Cash Per Share	US\$7.55	
Debt to Total Capital	0%	
Div (ann)	US\$0.00	
Fiscal Year End	Dec	

Price Performance - 1 Year



Source: Bloomberg

AAVL Upcoming Catalysts				
Program	Indication	Type	Event	Expected Timing
AVA-101	wet AMD	Clinical	P1 data from AGTC/Genzyme intravitreal gene therapy study	Oct 2014 (AAO)
		Clinical	P2a data, AVA-101 subretinal	Mid-2015
		Commercial	REGN 45d exclusivity to discuss licensing	Mid-2015
		Regulatory	File IND	Mid-2015
		Clinical	Start P2b study in U.S.	2H15
AVA-201	wet AMD	Clinical	File IND	2016
AVA-311	XLRS	Clinical	File IND	2016

Source: PJC and Company reports

AAVL DCF Analysis (2014-2024 CF Estimates)	
Discounted Cash Flow (DCF) Analysis	
Assumed Discount Rate (%)	11.0%
Terminal Growth Rate (%)	5.0%
Implied Terminal Year FCF Multiple	17.5x
NPV of FCF	\$1,004
Cash/equiv	\$163
Price Target	\$39
Target valuation	\$1,167
Shares Outstanding 2017E (million)	30.0

Source: PJC estimates

AAVL Valuation Sensitivity Analysis					
Terminal Growth	Discount Rate				
		10%	11%	12%	13%
	3.0%	\$36	\$29	\$23	\$19
	4.0%	\$43	\$33	\$26	\$21
	5.0%	\$52	\$39	\$30	\$24
	6.0%	\$65	\$47	\$35	\$27
	7.0%	\$88	\$59	\$43	\$32

Source: PJC estimates

AAVL Potential Upside From Current Levels					
Terminal Growth	Discount Rate				
		10.0%	11.0%	12.0%	13.0%
	3.0%	21%	(5%)	(23%)	(37%)
	4.0%	42%	10%	(13%)	(30%)
	5.0%	72%	29%	(0%)	(21%)
	6.0%	116%	56%	17%	(9%)
	7.0%	191%	96%	42%	7%

Source: Company Reports and Piper Jaffray.

AAVL QUARTERLY P&L											
	2013A	1Q14A	2Q14E	3Q14E	4Q14E	2014E	1Q15E	2Q15E	3Q15E	4Q15E	2015E
Product Revenue/Royalty	\$0	\$0	\$0	\$0	\$0	0.0	\$0	\$0	\$0	\$0	0
Funding/milestones	0.5	0.0	0.1	1.5	1.5	3.2	3	3	3	3	12
Total Revenue	\$0.5	\$0.03	\$0.14	\$1.50	\$1.50	\$3	\$3	\$3	\$3	\$3	\$12
COGS	0	0	0	0	0	0	0	0	0	0	0
<i>% product sales</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>
R&D	2	1	3	4	4	12	6	7	8	9	30
<i>% revenue</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>
SG&A	2	1	1	2	2	5	2	2	2	2	6
<i>% revenue</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>
Total operating expenses	4	2	5	6	6	17	8	9	10	11	36
Interest/other	-2	0	-1	0	0	-1	0	0	0	0	1
Pretax income	(\$5)	(\$2)	(\$5)	(\$4)	(\$4)	(\$15)	(\$4)	(\$5)	(\$6)	(\$7)	(\$23)
Taxes	0	0	0	0	0	0	0	0	0	0	0
<i>Tax rate</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>
Net income	-5	-2	-5	-4	-4	-15	-4	-5	-6	-7	-23
EPS	(\$0.74)	(\$0.11)	(\$0.28)	(\$0.18)	(\$0.18)	(\$0.77)	(\$0.18)	(\$0.22)	(\$0.26)	(\$0.30)	(\$0.97)
Shares	7	15	18	22	22	19	23	24	24	25	24

Sources: Company Reports and Piper Jaffray

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AAVL ANNUAL PRODUCT MODEL												
	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
AVA-101 Status	P1	P2a	P2b	P2b	P3	P3	Filing	Launch	Market	Market	Market	Market
AVA-201 Status	N/A	Preclin	Preclin	P1	P2	P2	P3	P3	Filing	Launch	Market	Market
AVA-311 Status	N/A	Preclin	Preclin	P1	P2/3	P2/3	P2/3	Filing	Launch	Market	Market	Market
Wet AMD eyes/yr, U.S. (000s)	100	100	101	102	103	104	105	106	107	108	109	110
<i>High frequency injection eyes</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>
<i>High frequency 101/201 penetr.</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>8%</i>	<i>20%</i>	<i>35%</i>	<i>45%</i>
<i>Mid frequency injection eyes</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>	<i>55%</i>
<i>Mid frequency 101/201 penetr.</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>1%</i>	<i>2%</i>	<i>4%</i>	<i>8%</i>	<i>12%</i>
AVA-101/201 injections (000s)	0	0	0	0	0	0	0	0	3	8	14	20
AVA-101/201 price/Rx (000s)	\$25	\$25	\$25	\$25	\$25	\$25	\$25	\$25	\$25	\$25	\$25	\$25
AVA-101/201 Sales (mm)	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$7	\$83	\$195	\$360	\$493
OUS AVA-101/201 Sales (mm)	0	0	0	0	0	0	0	0	0	50	100	200
<i>% Avalanche Royalty on OUS</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>	<i>15%</i>
AVA-101/201 Royalty, OUS (mm)	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$8	\$15	\$30
XLRS patients, W/W	20	20	20	20	20	20	20	20	20	20	20	20
<i>AVA-311 penetration</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>1%</i>	<i>3%</i>	<i>4%</i>	<i>6%</i>
AVA-311 price/Rx (000s)	\$150	\$150	\$150	\$150	\$150	\$150	\$150	\$150	\$150	\$150	\$150	\$150
AVA-311 sales	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$30	\$90	\$120	\$180
<i>% Avalanche Royalty on AVA-311</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>11%</i>
AVA-311 Royalty	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$3	\$9	\$12	\$20

Sources: Company Reports and Piper Jaffray

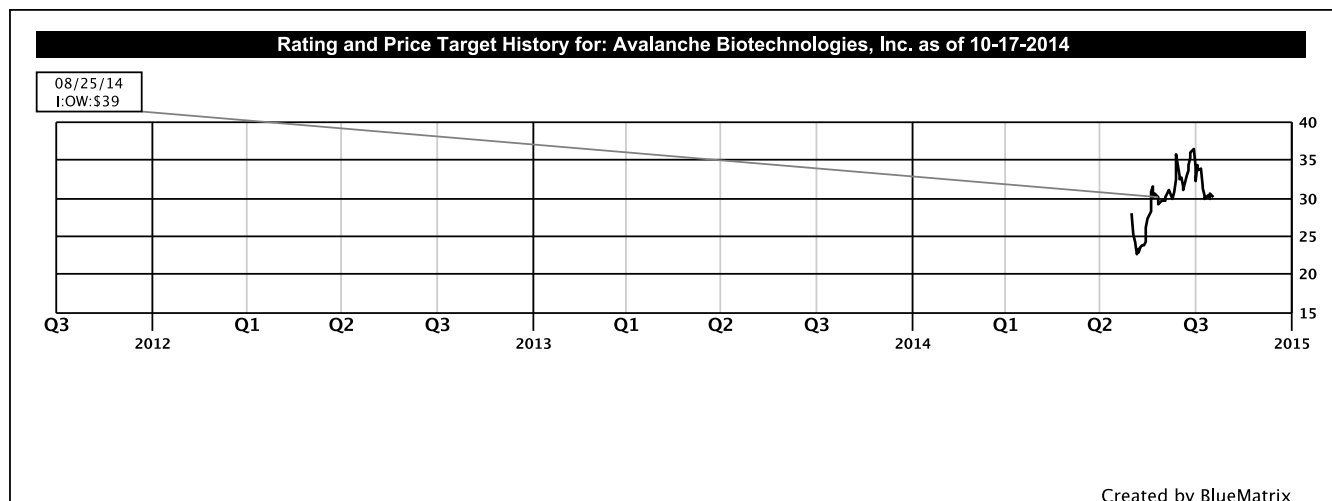
AAVL ANNUAL P&L												
	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Product Revenue/Royalty	\$0	0.0	0	\$0	\$0	\$0	\$0	\$7	\$86	\$211	\$387	\$543
Funding/milestones	0.5	3.2	12	12	12	12	12	12	12	12	12	12
Total Revenue	\$0.5	\$3	\$12	\$12	\$12	\$12	\$12	\$19	\$98	\$223	\$399	\$555
COGS	0	0	0	0	0	0	0	1	8	19	36	49
<i>% product sales</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>	<i>10%</i>
R&D	2	12	30	40	60	80	80	65	75	80	85	90
<i>% revenue</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>333%</i>	<i>500%</i>	<i>667%</i>	<i>667%</i>	<i>337%</i>	<i>76%</i>	<i>36%</i>	<i>21%</i>	<i>16%</i>
SG&A	2	5	6	8	10	10	12	80	100	125	135	145
<i>% revenue</i>	<i>N/M</i>	<i>N/M</i>	<i>N/M</i>	<i>67%</i>	<i>83%</i>	<i>83%</i>	<i>100%</i>	<i>415%</i>	<i>102%</i>	<i>56%</i>	<i>34%</i>	<i>26%</i>
Total operating expenses	4	17	36	48	70	90	92	146	183	224	256	284
Interest/other	-2	-1	1	1	1	1	1	1	1	2	4	6
Pretax income	(\$5)	(\$15)	(\$23)	(\$35)	(\$57)	(\$77)	(\$79)	(\$125)	(\$84)	\$1	\$147	\$276
Taxes	0	0	0	0	0	0	0	0	0	0	37	69
<i>Tax rate</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>0%</i>	<i>25%</i>	<i>25%</i>	<i>25%</i>
Net income	-5	-15	-23	-35	-57	-77	-79	-125	-84	1	110	207
EPS	(\$0.74)	(\$0.77)	(\$0.97)	(\$1.35)	(\$1.90)	(\$2.41)	(\$2.08)	(\$3.14)	(\$2.01)	\$0.02	\$2.29	\$4.15
Shares	7	19	24	26	30	32	38	40	42	46	48	50

Sources: Company Reports and Piper Jaffray

AAVL STATEMENT OF CASH FLOWS												
	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E
Net Income	-5	-15	-23	-35	-57	-77	-79	-125.43	-84	1	110	207
Depreciation	0	0	0	0	0	0	0	0	0	0	0	0
Stock based comp	1	5	8	10	12	14	16	18	20	22	24	25
Other	3	0	0	0	0	0	0	0	0	0	0	0
Change in NWC	0	-2	-4	-4	-5	-10	-15	-15	-15	-15	-15	0
Cash from operations	-2	-11	-19	-29	-50	-73	-78	-122.43	-79	8	119	232
PP&E	0	0	0	-2	-2	-2	-2	-2	-2	-2	-2	-2
Free cash flow	-2	-11	-19	-31	-52	-75	-80	-124.43	-81	6	117	230
Financing Cash	2.48	173.3	0	0	125	0	175	0	0	0	0	0
Cash start	0	1	162	143	112	185	110	205	81	0	6	122
Cash end	1	162	143	112	185	110	205	81	0	6	122	353

Sources: Company Reports and Piper Jaffray

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R: Resuming Coverage
T: Transferring Coverage
D: Discontinuing Coverage
S: Suspending Coverage
OW: Overweight
N: Neutral
UW: Underweight
NA: Not Available
UR: Under Review

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			Count	Percent

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Analyst Certification — Joshua E. Schimmer, MD, Sr Research Analyst
— Jerry Yang, Ph.D., Research Analyst

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