

## Avalanche Biotechnologies (AAVL) Genzyme Gene Therapy Data Underwhelms

**BUY**

Price target \$40.00

Price \$32.43

### Key Takeaway

**Earlier this afternoon at the annual meeting of the Retina Society, Genzyme presented PI data from its AAV2-sFLT01 gene therapy for wet AMD in 19 patients, and reported 3.7 letter gained over baseline w/ the highest dose group observing a 4.7 letter gain over baseline. The data appears to underwhelm w/ the lead investigator suggesting that the dose may not have been optimized, and higher doses could improve the efficacy profile.**

**Genzyme PI Data In Wet AMD:** Genzyme, a Sanofi company (SAN FP, €86.89, Buy) is developing an intravitreally-delivered AAV2-sFLT01 product for wAMD, likely the closest competitor to AAVL's AVA-101. Genzyme presented PI data on Fri which was a study of 19 wAMD pts, 7 of which were in MTD cohort. In all cohorts, the mean VA change was +3.7 letters, and mean change in central retinal thickness (CRT) was -91.5 microns on OCT. For the MTD cohort, the mean VA was +4.7 letters, and mean change in CRT was -155 microns. We had hoped the data would have included monthly changes to 12 mos in order to assess whether responders were in fact improving over the course of the 12 mos but these datasets were not presented. Four patients observed at least a 20% improvement in retinal fluid and required no rescue therapy. The overall nos. of pts that required rescue therapy were not disclosed. On safety, there was 1 intraocular inflammation event at the high dose which resolved at week 5 after tx w/ steroid eye drops. Heier believes the dose may be pushed higher b/c significant inflammation was not observed, and may help w/ VA improvement. Also, limited baseline data were provided w/ median age of 76 y/o and duration of disease was 5.4 years. The trial was a 2-stage w/ the 1st stage enrolling end-stage pts w/ scarring in the macula and stage 2 enrolling pts w/ evidence of VEGF response.

**Topline PIIa Trial Data for AVA-101 in Mid-'15:** AAVL's lead candidate is AVA-101, a one-time subretinal injection which offers durable remission for pts with wAMD. AVA-101 has already reported impressive efficacy and safety results from 8 pts from its PI study. Pts enrolled in the study were limited to subjects 55 yrs or older (median age of 79 yrs) and baseline VA ranged from 28-56 letters. Mean VA improvement from baseline were +8.7 and +6.3 letters for the low- ( $1 \times 10^{10}$  vg) and high-dose ( $1 \times 10^{11}$  vg), respectively, compared to -3.5 letters from control at wk 52. Thus, mean VA improvement in the +12.2 and +9.8 letters for the low- and high-dose, respectively, v. control. Impressively, fewer pts on AVA-101 required Lucentis re-tx (eligible every 4 wks) relative to the control (0.33 v. 3.0, respectively) ( $p < 0.001$ ). The effect appears durable lasting >12 mos, and potentially for many years. Moreover, the central retinal thickness was found to have improved and maintained through the 12 mo period (mean change from baseline of ~200 microns). The PIIa trial has enrolled 32 pts, and we await topline data in mid-'15. AAVL also has potential to expand into DME and CRVO.

**Biren Amin \***

Equity Analyst

(212) 284-8162 bamin@jefferies.com

**Hugo Ong, Ph.D. \***

Equity Associate

(212) 323-3364 hong@jefferies.com

**Sridhar Vempati, PhD \***

Equity Associate

(212) 284-2535 svempati@jefferies.com

\* Jefferies LLC

## Company Description

Avalanche Biotechnologies, Inc., a clinical-stage biotechnology company, focuses on discovering and developing novel gene therapies for the treatment of ophthalmic diseases based on its Ocular BioFactory platform. Its lead product candidate includes AVA-101, which is in a Phase I/IIa trial for the treatment of wet age-related macular degeneration (AMD). The company is also developing AVA-201, an anti-vascular endothelial growth factor gene therapy product candidate for the prevention of wet AMD; and AVA-311 that is in preclinical studies for the treatment of juvenile X-linked retinoschisis, a rare genetic disease of the retina with no approved therapy. Avalanche Biotechnologies, Inc. has a collaboration agreement with Regeneron Pharmaceuticals, Inc. research, develop, and commercialize gene therapy products. The company was founded in 2006 and is headquartered in Menlo Park, California.

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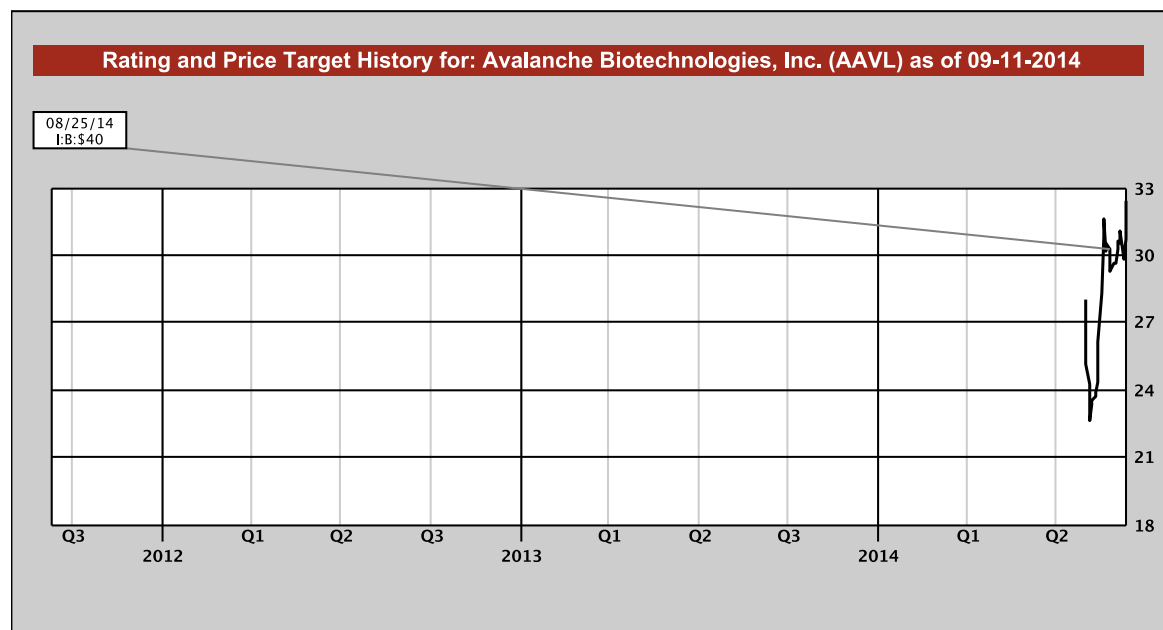
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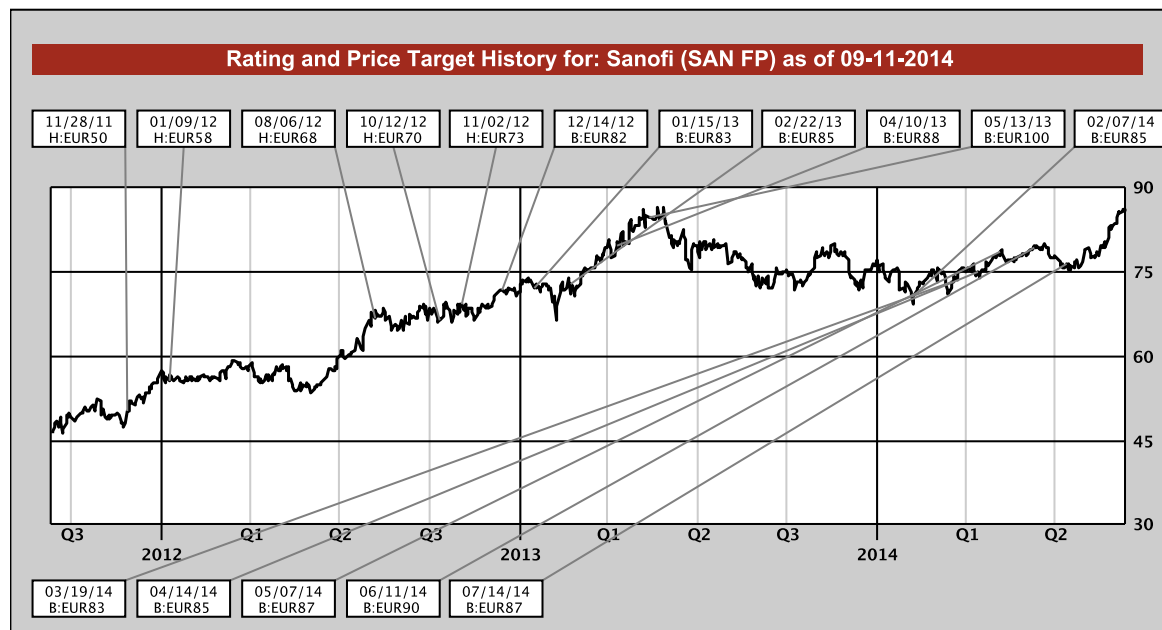
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- Sanofi (SAN FP: €86.89, BUY)





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			Count	Percent
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