Avalanche Biotechnologies (AAVL) — Overweight

AVA-101 Data Controversial; Let The Debate Begin

CONCLUSION

After the close, AAVL reported the highly anticipated results of the P2a for gene therapy AVA-101 for treatment of wet AMD. Investor reaction has been extremely and vociferously mixed (although skewed bearish) given the odd OCT data and median Lucentis injection frequency reduction of 2, and there is not an interpretation which will satisfy everyone. Overall, it's still early, but the data is largely in line with our expectations, showing what we believe is real biological activity in a subset of responders with a meaningful reduction in injection frequency, along with improvements in BCVA, but also with plenty of room for improvement. Our overall positive outlook for AAVL looks beyond this data and towards its expanding gene therapy pipeline and vector evolution strategy, which is underappreciated in our view. Reiterate OW.

- **It's early people**: Investors clamoring to over-interpret this early data are likely to run into dead ends. It is a small trial demonstrating safety and evidence of biologic activity, but leaving plenty of room for improvement. While many have expressed disappointment in management's handling of the results release and call, there is only so much they could do with an early limited dataset; don't hate the player, hate the game. We recommend jets be cooled and the company be given the opportunity to hone in on a group of wet AMD patients most likely to respond to '101 therapy in the upcoming P2b trial and to further analyze these P2a results. While there may be a limited amount of NT newsflow for AVA-101 (data presentation and REGN's right of first negotiation), this is an opportunity to shift investor focus to the emerging pipeline and novel vectors and promoters which represent the future of gene therapy anyways.

- **Subset of responders with BCVA gains:** The trial largely enrolled a difficult to treat patient population who required repeated injections of Lucentis, in contrast to most other Lucentis all-comers trials, precluding effective cross trial comparisons. We previously highlighted the goal of reducing injection frequency in a meaningful proportion of patients. Overall, 52% of patients required ≤2 rescue injections compared to 9% in the control group. While this is slightly below our expectations (we had been hoping for 40-50% with 0-1 injections/YE) it is offset by gains in visual acuity which had not been part of our expectations and thus still represents a meaningful improvement in our view as long as therapy is safe. 43% of treated patients treated with '101 had improved or stable vision with ≤2 rescue injections compared to 9% in the control group. Furthermore, BCVA improvements of ≥10 letters with ≤2 rescue injections was observed in 24% of treated patients vs 0% in the control group, a further signal of efficacy which we believe represents a true benefit of the procedure.

- **OCT data difficult to interpret:** The 25 μm increase in the treated arm vs a 56 μm drop in the control arm is a primary source of investor concern. The difference is not clinically meaningful in our view and OCT is not a registration endpoint so we caution against over-interpretation of this signal. AAVL also noted baseline imbalances. That said, this is something to keep an eye on with longer term follow up and future studies.

COMPANY DESCRIPTION

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

PRICE: US$38.88
TARGET: US$52.00
DCF thru 2024, 11% discount rate, 6.5% terminal growth rate

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RISKS TO ACHIEVEMENT OF PRICE TARGET

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

Price Performance - 1 Year

Source: Bloomberg

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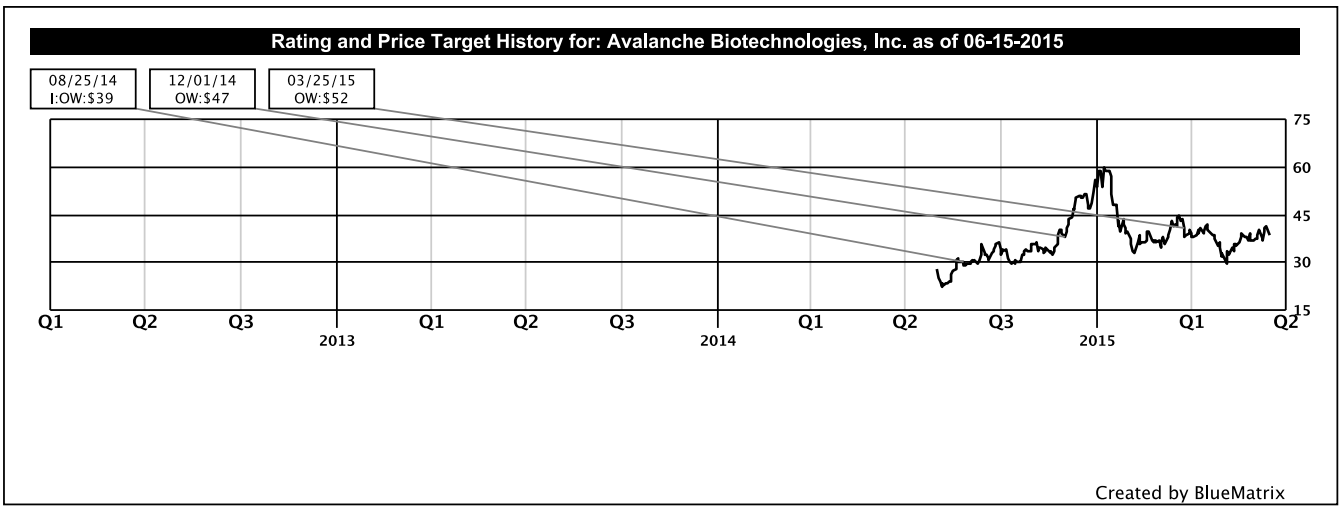

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N: Neutral
UW: Underweight
NA: Not Available
UR: Under Review

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