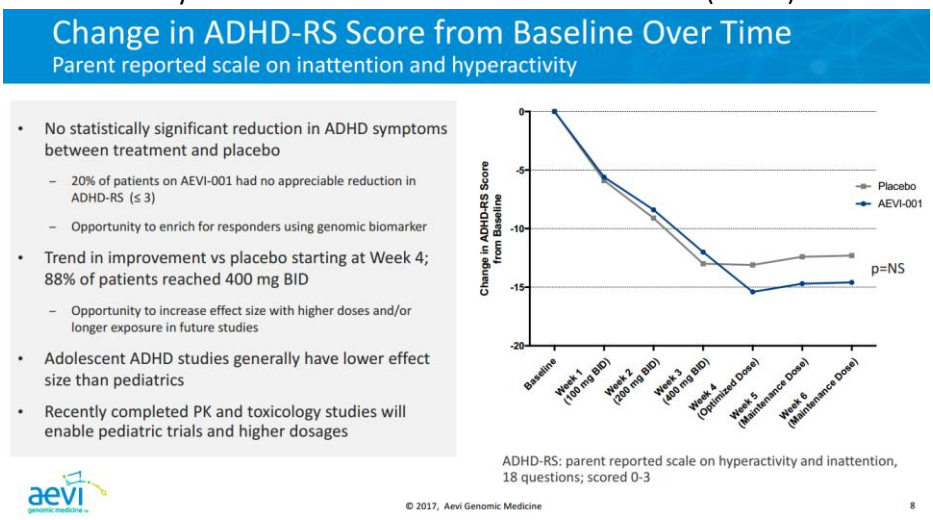
My Thoughts on AEVI-001 SAGA Top-line Data

Written by: Zack Fink

I have had people reaching out to me throughout the day for my thoughts on the AEVI-001 SAGA data, however, I did not want to comment until I had a chance to speak with management and re-listen to the conference call. What you will find below are my brief thoughts on these data and what Aevi Genomics can do to hopefully come out with a positive outcome in future trials. What you will not find below is an apology for owning a stock that goes down or for not sharing my thoughts on these data sooner. I have for years shared my due diligence on numerous investments/ideas. I "own" my investments for better or worse. I take it as a huge insult that after all the research I have shared, that people would think I am "ducking" this event because it didn't have the outcome I hoped for.

Efficacy Summary

In the SAGA phase II/III study, AEVI-001 failed to show a statistically significant separation from placebo as measured by reduction in ADHD-RS score from baseline (below).

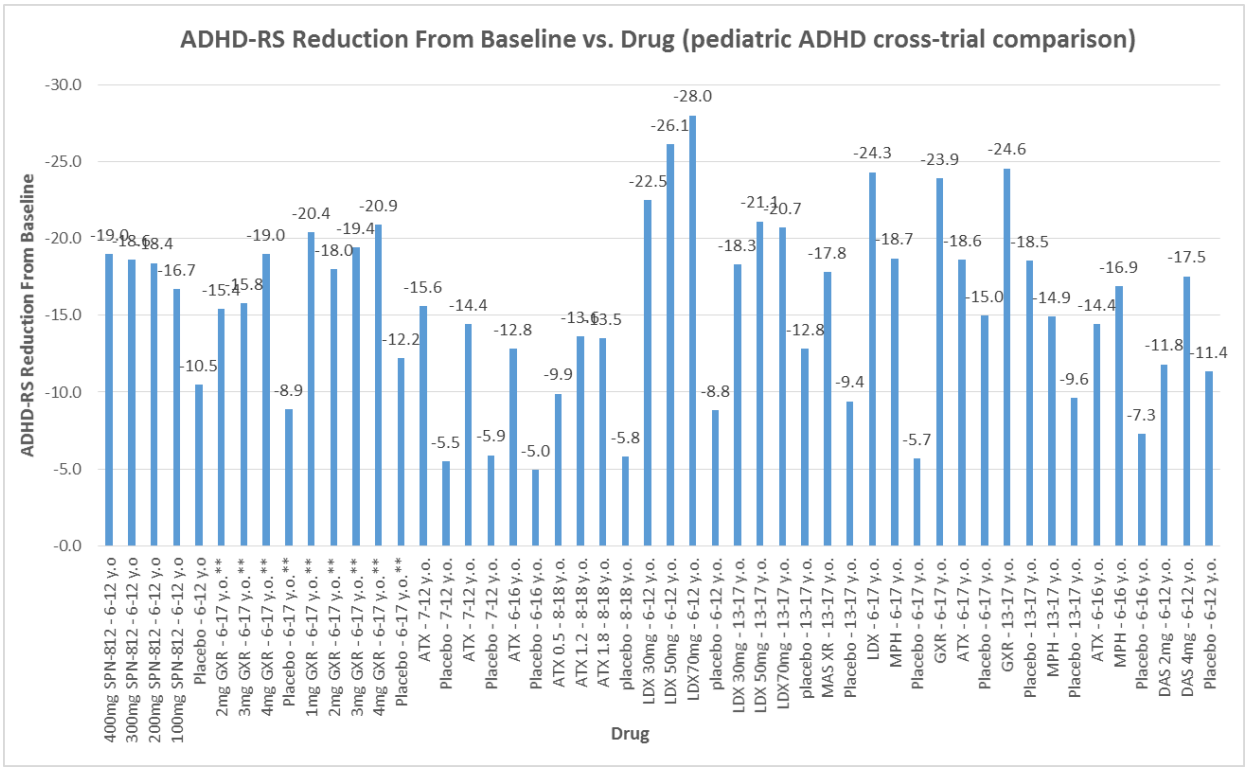


Despite this trial being a failure as assessed by the primary endpoint, I believe AEVI-001 demonstrated an efficacy signal in a subset of patients and a clean safety profile. This is evident by the responder analysis for ADHD-RS (>30% reduction in ADHD-RS) and CGI-I (CGI-I of 1 or 2). At week 6, AEVI-001 and placebo had an ADHD-RS response rate of 70% and 42% (p=0.0067), respectively. Response rates at week 6 measured by CGI-I were 57% and 33% (p=0.0155) for AEVI-001 and placebo. This compares favorably to Concerta (methylphenidate) which demonstrated response rates in an adolescent ADHD study of 73.3% for ADHD-RS and 51.8% for CGI-I [1].

Importantly, for the 70% responders, the absolute reduction from baseline in ADHD-RS was over 19 points. This contrasts with 20% of the AEVI-001 treatment group demonstrating an absolute ADHD-RS reduction of ≤ 3. In addition, it appears there is a large enough therapeutic window that AEVI-001 can be dosed higher (more on the safety profile below). Looking at these data, it is reasonable to believe a higher dose could lead to a greater ADHD-RS reduction from baseline. These two points, in addition to a placebo response on the higher end of the expect range (more on this below), could explain why AEVI-

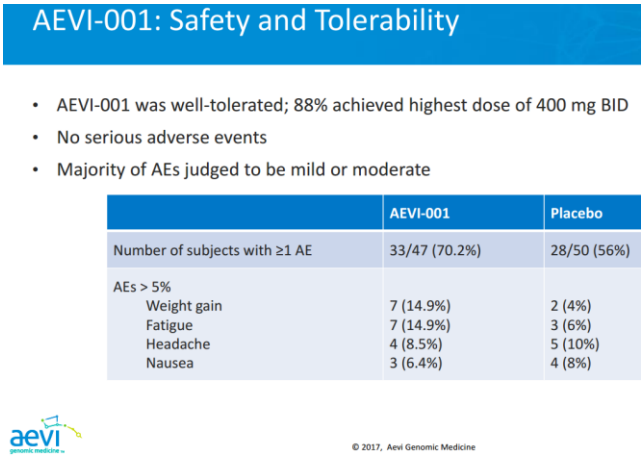
001 failed this trial, yet could still be an efficacious treatment option for a subset of patients with pediatric ADHD.

Going forward, the two key modifications I believe Aevi Genomics can leverage are refining the mGluR+ biomarker (screening out severe non-responders), and increasing the dose in their guided pediatric (ages 6-12) phase II trial. Although a potential lower placebo response in patients ages 6-12 could be a benefit (below), I believe the key levers Aevi has to pull are screening out the severe non-responders and increasing the dose. It is also worth mentioning that Aevi could potentially leverage the non-interventional trial data for these patients to further bolster the case for any modifications they choose to make going forward.



Safety Summary

In the SAGA trial, AEVI-001 demonstrated a clean safety profile (below), which should allow for higher dosing (>400mg BID). I believe briefly putting these safety data into context with approved ADHD drugs is worthwhile because it demonstrates that even if AEVI-001 is on par with approved non-stimulants efficacy-wise, it can still be a viable treatment option. In addition, it also provides some context as to why Aevi believes they can dose higher.



Stimulants (depending on the exact drug) can be associated with safety risks and side effects such

as cardiovascular risks, decreased appetite, addiction, and/or insomnia. As for non-stimulants, depending on the exact drug, these can be associated with somnolence, psychiatric AEs, and/or decreased appetite. Of these common AEs associated with approved stimulant and non-stimulant drugs – many of which have black box warnings (some for reasons not mentioned here) – it appears AEVI-001 does not lead to these AEs or risks.

Conclusion and Moving Forward

I believe AEVI-001 is not dead in the water. There are reasonable strategies/improvements – such as genetically screening out non-responders and upping the dose – which Aevi can potentially leverage to clearly demonstrate in future trials that AEVI-001 is an efficacious drug for a subset of patients with pediatric ADHD. I look forward to additional data from this trial at the World Congress on ADHD April 20-23, and importantly, any update on the genetic analysis.

Considering where Aevi Genomics is currently trading, I believe from a long-term perspective, the stock is undervalued considering the key value drivers such as their CAG collaboration. However, further discussion on these points is outside the scope of this post.