Title: Sodium vanadate combined with L-ascorbic acid delays disease progression, enhances motor performance, and ameliorates muscle atrophy and weakness in mice with spinal muscular atrophy

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Reviewer: Matthew E. R. Butchbach

Reviewer's report:

Major Compulsory Revisions

1. Please provide a rationale for using the PND1-30 treatment window for this study.

2. Why was this model of SMA selected for this preclinical trial instead of one of the early-onset SMA mouse models?

3. In the description of the gem analysis results, there are no error measurements provided in the results sections (pg 17). Please provide these error measurements.

4. While the effect of ascorbic acid on rescuing vanadate-induced toxicity is interesting, its prominent placement in the results section could confuse the reader. The figure showing this rescue of vanadate toxicity (Fig 3B) should be removed from the main manuscript and be included as a supplementary figure.

5. The scale on the y-axis of Figure 4B is not uniform and it should be. Additionally, the body mass data for ~PND10-PND24 WT mice are missing from the graph.

6. The authors mention that "several studies have demonstrated that early drug intervention yields more promising therapeutic effects in SMA mouse models." One of seminal papers that supports this premise, however, is not referenced (the quinazoline study published in HMG in 2010). This paper should be cited in this manuscript.

Minor Essential Revisions

1. The first subsection header in the results section ("L-AA has minor efficacy of SV of inducing SMN protein") should be more clearly worded.

2. In the methods sections, the negative geotaxis assay was first described in reference #48, not #49. Please correct.

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.