S1

| Genotype | Pupation (%) | Eclosion (%) |
|---|---|---|
| *Flag-Smn$^{WT}$,Smn$^{X7}$/Smn$^{X7}$* | 99 | 73 |
| *Flag-vSmn,Smn$^{X7}$/Smn$^{X7}$* | 86 | 83 |
| *Flag-vSmn$^{S201A}$,Smn$^{X7}$/Smn$^{X7}$* | 100 | 97.5 |

**Figure S1:** A) Transgenic flies expressing Flag-vSmn and Flag-vSmn$^{S201A}$ in the background of an *Smn$^{X7}$* null mutation are fully viable. The eclosion frequencies of these animals are consistently higher than those that express Flag-Smn$^{WT}$ in the background of an *Smn$^{X7}$* null mutation. The data for each genotype are expressed as a fraction of pupae or adults over the total number of starting larvae, n=200.

S2

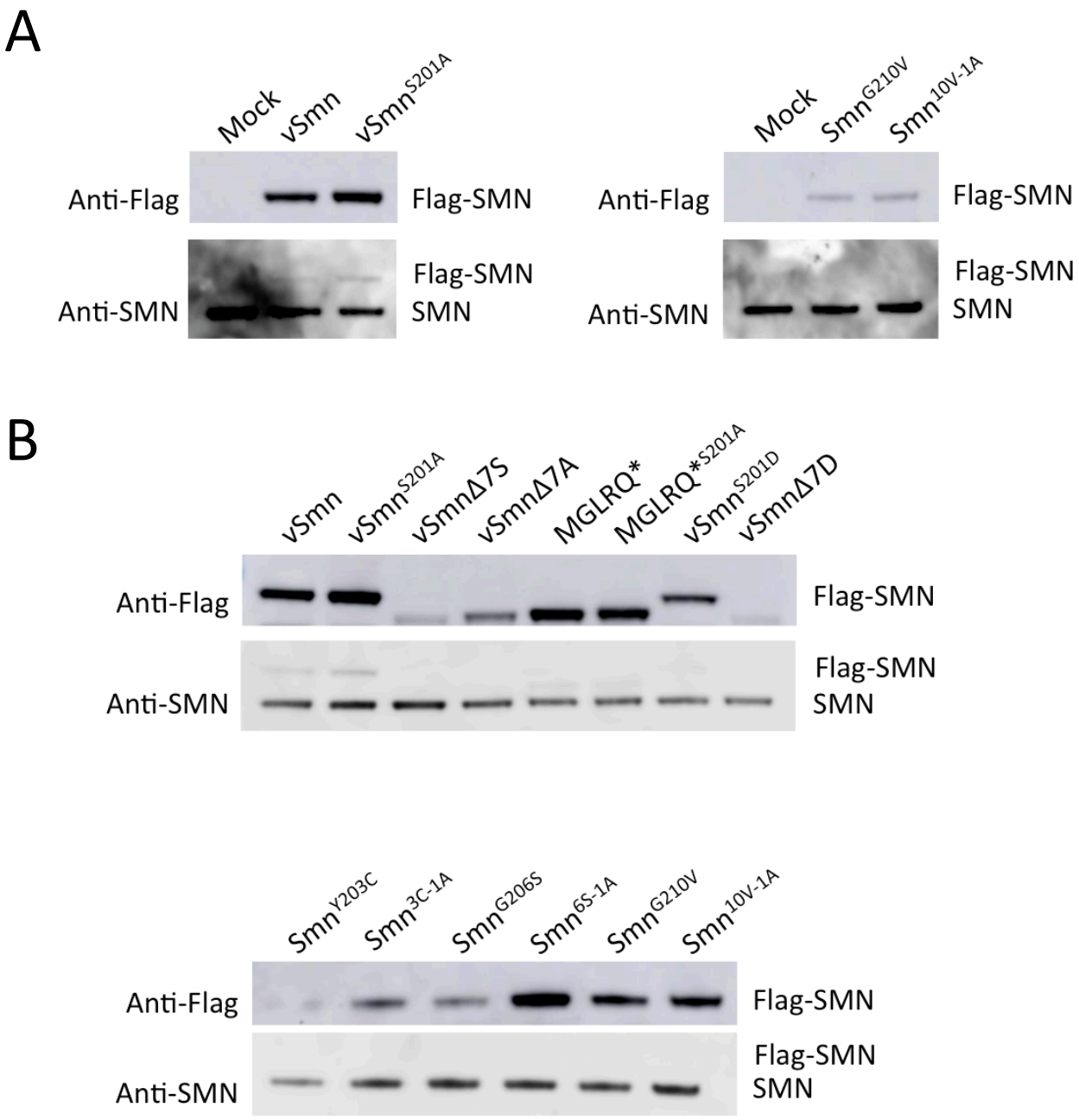


**Figure S2:** A) The expression of endogenous SMN in S2 cells following transient transfection of either modified 'vertebrate' SMN constructs (vSMN and vSMN$^{S201A}$) or Drosophila SMN constructs (Smn$^{G210V}$ and Smn$^{10V-1A}$) is unaffected, as compared to mock transfection. Protein is detected by anti-Flag antibody or anti-SMN antibody as indicated to the left of the blots. B) Transient transfections in S2 cells express Flag-SMN from the endogenous promoter. Protein levels of all transfected constructs are lower than endogenous SMN protein levels. Protein is detected by anti-Flag antibody or anti-SMN antibody as indicated to the left of the blots.

S3

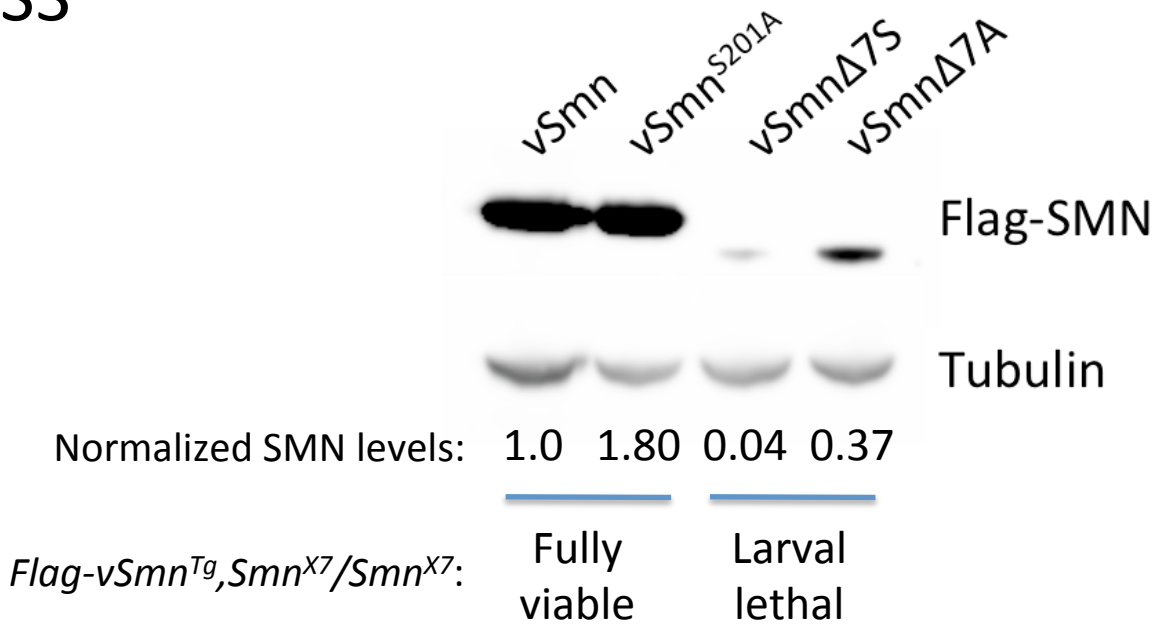


**Figure S3:** Western blotting was used to determine protein levels of each of the SMN constructs, with expression driven by the endogenous promoter, in transgenic adult flies. Protein lysates were made by pooling 40-50 adult flies. Flies with the following genotypes were analyzed in this experiment: *Flag-vSmn,Smn$^{X7}$/Tm6b* (vSmn), *Flag-vSmn$^{S201A}$,Smn$^{X7}$/Tm6b* (vSmn$^{S201A}$), *Flag-vSmnΔ7S,Smn$^{X7}$/Tm6b* (vSmnΔ7S) or *Flag-vSmnΔ7A,Smn$^{X7}$/Tm6b* (vSmnΔ7A). Both the vSMN and vSMNΔ7S proteins show increased levels when the serine is mutated to an alanine, indicating disruption of the normal degradation of SMN. Flag-SMN was detected using anti-Flag antibody. Normalized fold change as compared to vSmn levels is indicated at the bottom.

S4

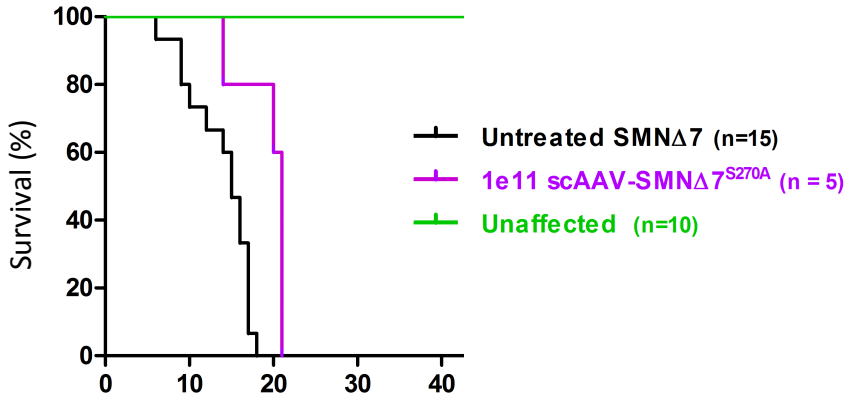


**Figure S4:** Survival analysis of the effects of SMNΔ7A expression in the severe Delta7 mouse model. Genotypes include untreated SMNΔ7 mice, which are a severe mouse model of SMA, SMNΔ7 mice treated with scAAV9 expressing SMNΔ7$^{S270A}$, truncated SMN with the S to A change in the degron, and control unaffected mice, which have a wild-type Smn allele. Treatment with AAV9-SMNΔ7A had only a very modest effect on viability and none of the animals survived weaning. 1e11 denotes the viral dose.

# S5

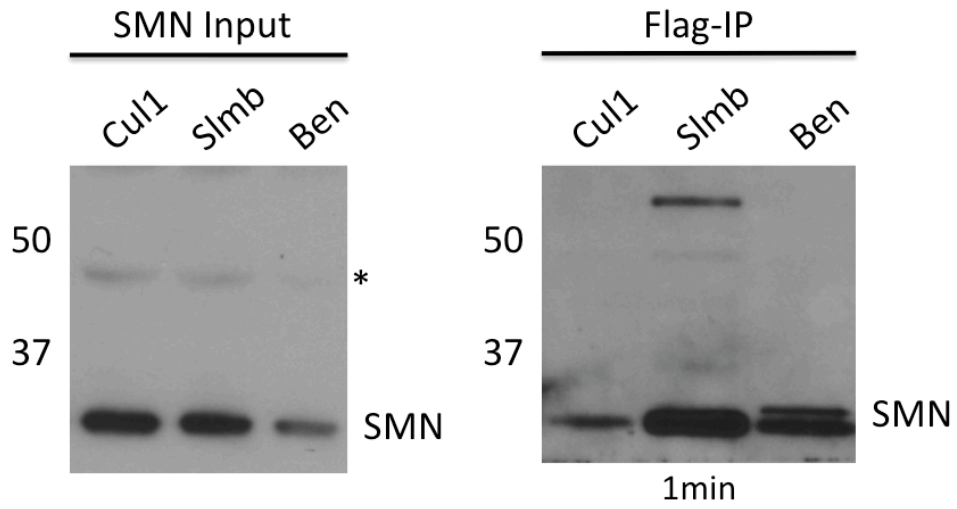


**Figure S5:** The interaction of SMN with Bendless (Ben) was validated in a co-immunoprecipitation assay. Following Cul1-Flag, Flag-Slmb, and Ben-Flag immunoprecipitation from Drosophila S2 cell lysates, western analysis using anti-SMN antibody for endogenous SMN was carried out. Flag-tagged Ben interacts with endogenous SMN. SMN interaction with Flag-Slmb was used as a positive control for protein interaction. * is a non-specific band detected by the Drosophila SMN antibody.