Representative Western blot showing the effect of PRL on SMN protein in muscle samples of SMAΔ7 mice treated with Saline (control, lane 1,2 & 3) or PRL (lane 4, 5, 6 & 7) (each lane represents individual animal). (f) Densitometric quantification of SMN relative to Tubulin [mean + SD (bars)] is shown for muscle samples.

**Figure 8. Proposed Model for PRL-mediated induction of SMN in motor neurons.** PRL treatment causes phosphorylation and activation of STAT5 pathway which results in transcriptional upregulation of SMN gene, resulting in an increase in SMN mRNA levels and ultimately increases SMN protein expression.

**Supplemental figure 1. PRL dose optimization for SMN induction in SMA mice model.** SMAΔ7 mice were treated daily with PRL (0.5 and 2.5 mg/kg) from P1 for 6 days, then sacrificed at P7. Brain and spinal cord tissues were harvested Western blot analysis. (a) Representative Western blot showing effect of PRL on SMN protein in brain samples of SMAΔ7 mice treated with Saline (control, lane 1) or PRL (0.5 & 2.5 mg/kg; lane 2 & 3 respectively) (each lane represents individual animal). (b) Representative Western blot showing effect of PRL on SMN protein in spinal cord samples of SMAΔ7 mice treated with Saline (control, lane 1) or PRL (0.5 & 2.5 mg/kg; lane 2 & 3 respectively) (each lane represents individual animal).

**Supplemental figure 2. PRL treatment does not affect SMN protein level in heart tissues of SMAΔ7 mice until time of death.** SMAΔ7 mice were treated
daily with PRL (2.5 mg/kg) from P1 onward. Heart tissues were harvested upon death for Western blot analysis. (a) Representative Western blot showing the effect of PRL on SMN protein in heart samples of SMAΔ7 mice treated with saline (control, lane 1, 2 & 3) or PRL (lane 4, 5 & 6).

Supplemental figure 3. Genotyping of transgenic mice using two different primer sets.

Supplemental figure 4. Comparison of SMN induction in SMA mice model (mSmn-/-;hSMN2+/+, hSMNΔ7+/+) after PRL treatment with carrier treated heterozygous transgenic mice (mSmn+/−;hSMN2+/+, hSMNΔ7+/+). SMAΔ7 and heterozygous mice were treated daily with saline or PRL (2.5 mg/kg; SMAΔ7 mice only) from P1 for 6 days, then sacrificed at P7. Brain and spinal cord tissues were harvested Western blot analysis. (a) Representative Western blot showing effect of PRL on SMN protein in brain samples of SMAΔ7 and heterozygous mice treated with Saline (control, lane 1 & 3 respectively) or PRL (2.5 mg/kg; lane 2) (each lane represents individual animal). (a) Representative Western blot showing effect of PRL on SMN protein in spinal cord samples of SMAΔ7 and heterozygous mice treated with Saline (control, lane 1 & 3 respectively) or PRL (2.5 mg/kg; lane 2) (each lane represents individual animal).
Supplementary figure 5. Comparison of SMN induction in motor neurons in SMA mice model (mSmn-/-;hSMN2+/+, hSMNΔ7+/+) after PRL treatment with carrier treated heterozygous transgenic mice (mSmn+/--;hSMN2+/+, hSMNΔ7+/+). SMAΔ7 and heterozygous mice were treated daily with saline or PRL (2.5 mg/kg; SMAΔ7 mice only) from P1 for 6 days, then sacrificed at P7. Brain tissues were harvested for Immunohistochemistry analysis. Representative merged Confocal images [SMN/alexa488 (green) + HB9/alexa 568 (red; motor neuron marker) + Hoechst (blue)] for different tissues are shown. Representative Confocal images showing effect of PRL on SMN protein expression in brain stem motor neurons samples of SMAΔ7 and heterozygous mice treated with Saline (A & C respectively) or PRL (B). Scale bars: 10μM.

**Supplemental videos.** PRL treatment ameliorates on disease phenotype in SMA mice model. (a) P13 SMA mice (control; saline treated). (b) P21 SMA mice (PRL-treated). (c) P13 untreated heterozygous mice.
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Supplemental Figure 2
Supplemental Figure 3

**2 primer set: lac Z and mSMN**

- a-SMA
- b-HET
- c-WT
- d-HET
- e-SMA
- f-WT
- g-HET
- h-HET
- i-HET

Lac Z (626 bp)

mSMN (372 bp)

**1 primer set: mSMN**

- a-SMA
- b-HET or WT
- c-HET or WT
- d-HET or WT
- e-SMA
- f-HET or WT
- g-HET or WT
- h-HET or WT
- i-HET or WT

mSMN (500 bp)
Supplemental Figure 4
Supplemental Figure 5

A: SMA-Saline
B: SMA-PRL
C: Heterozygous

Brain