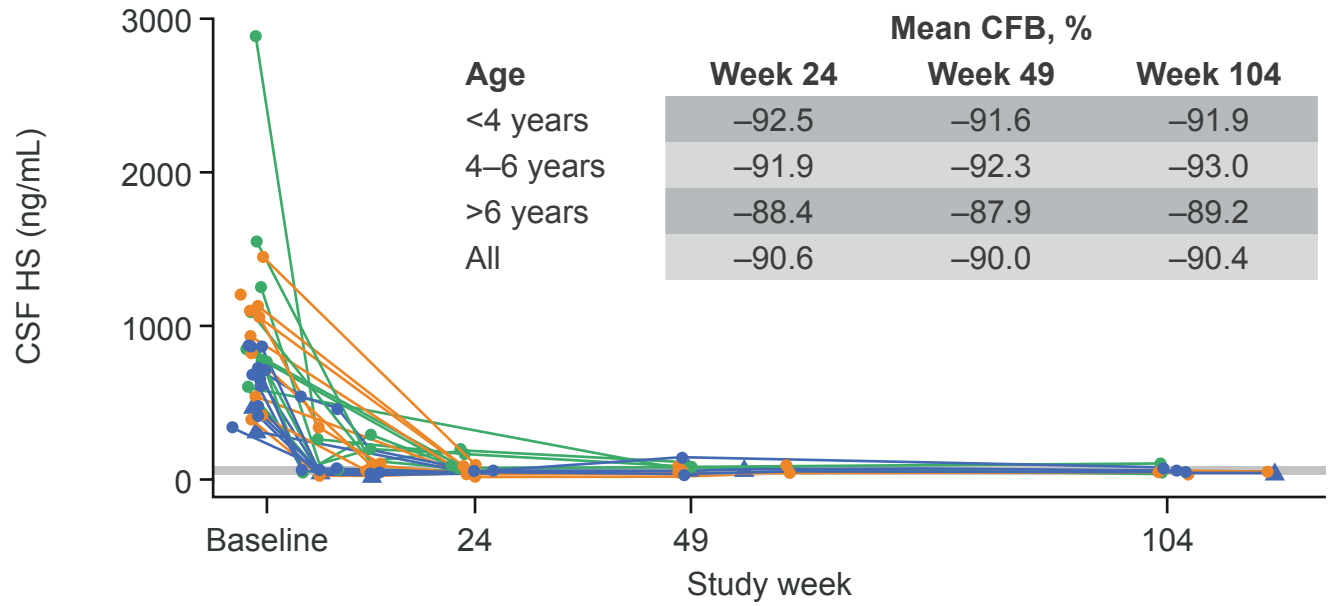
Supplemental Table 1. Baseline demographics and disease characteristics of participants

	Cohorts A–E (n=37)
Age	
Category, n (%)	
<4 years	10 (27.0)
4–6 years	12 (32.4)
>6 years	15 (40.5)
Median (min–max), years	5.1 (1.8–12.6)
MPS II phenotype, n (%)	
Neuronopathic	34 (91.9)
Non-neuronopathic	3 (8.1)
Variant type, n (%)	
Missense/synonymous	19 (51.4)
Large deletions/rearrangement	5 (13.5)
Other[a]	13 (35.1)
ERT status at enrollment	
SOC ERT-naive,[b] n (%)	10 (27.0)
SOC ERT-exposed, n (%)	27 (73.0)
Duration of SOC ERT, median (min–max), years[c]	2.2 (0.4–11.2)
Race, n (%)	
Asian	4 (10.8)
Black or African American	1 (2.7)
White	21 (56.8)
Not reported, unknown or other	11 (29.7)
Ethnicity, n (%)	
Hispanic or Latino	6 (16.2)
Not Hispanic or Latino	29 (78.4)
Not reported	2 (5.4)

Data are presented for the safety population. [a]Includes nonsense and splice site/intron. [b]Includes one participant who underwent allogeneic hematopoietic stem cell transplantation. [c]n=26. ERT, enzyme replacement therapy; max, maximum; min, minimum; MPS II, mucopolysaccharidosis type II; SOC, standard of care.

Supplemental Figure 1. CSF HS levels with tividenofusp alfa treatment[a]

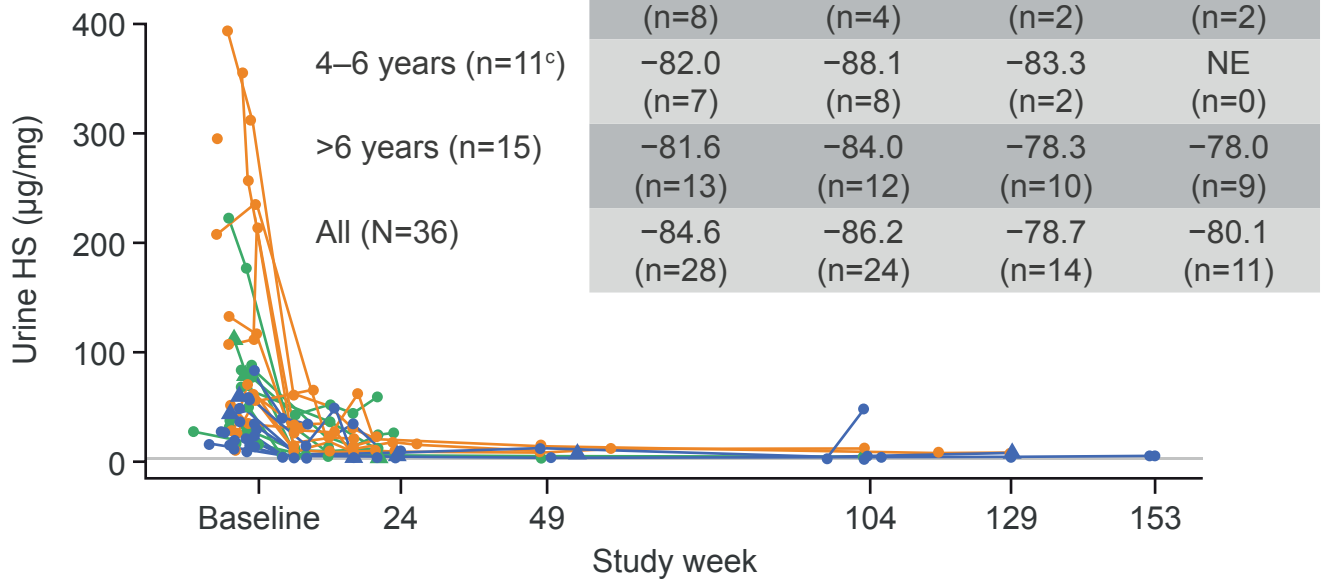


Age	Mean CFB, % Week 24	Week 49	Week 104
<4 years	–92.5	–91.6	–91.9
4–6 years	–91.9	–92.3	–93.0
>6 years	–88.4	–87.9	–89.2
All	–90.6	–90.0	–90.4

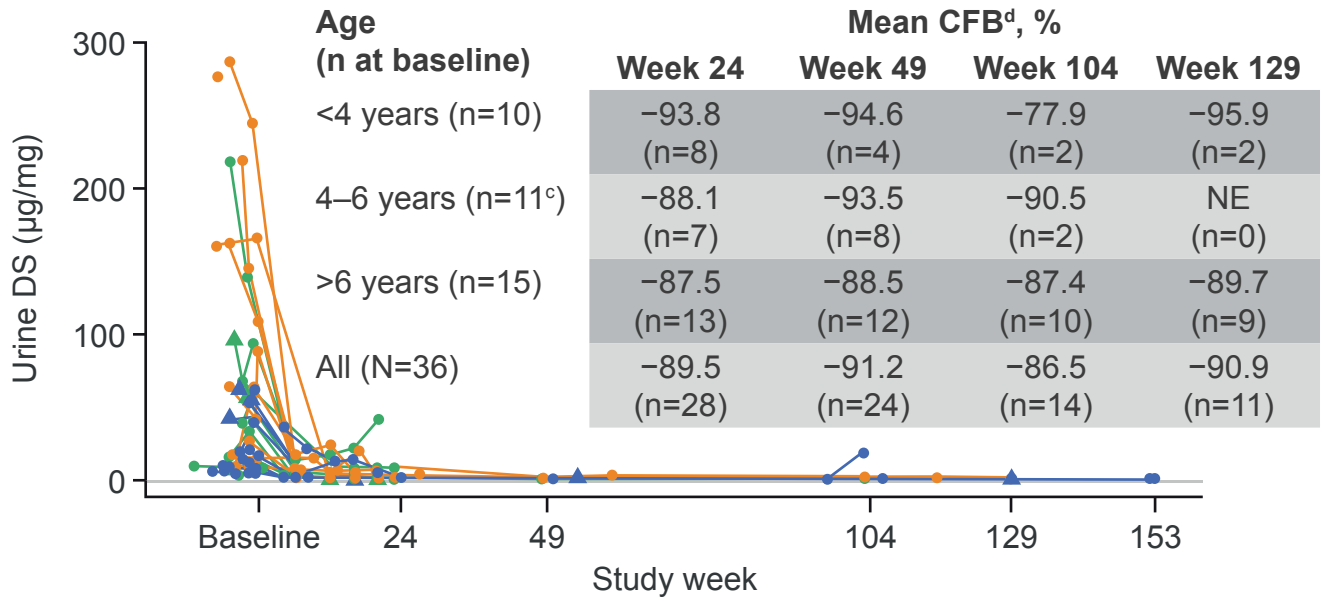
Number of participants, n	Baseline	24	49	104
<4 years	10	9	6	3
4–6 years	11	9	8	3
>6 years	15	13	13	10
All	36	31	27	16

[a]Shaded gray area indicates the preliminary normal range of 39.1–92.5 ng/mL (10th to 90th percentiles) based on an analysis of CSF samples from 30 healthy adults (median [range] age, 52 [18–81] years). Total CSF GAG levels are similar in adults and children.[1] CFB, change from baseline; CSF, cerebrospinal fluid; GAG, glycosaminoglycan; HS, heparan sulfate; MPS II, mucopolysaccharidosis type II.

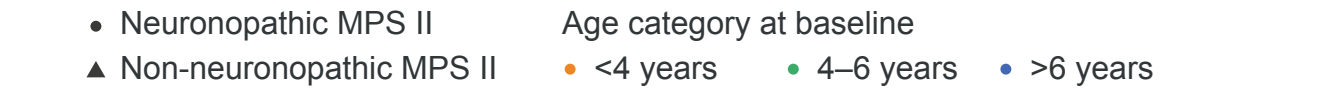
Supplemental Figure 2. Urine (A) HS[a] and (B) DS[b] levels with tividenofusp alfa treatment



Age (n at baseline)	Mean CFB[d], %			
	Week 24	Week 49	Week 104	Week 129
<4 years (n=10)	−91.8 (n=8)	−89.3 (n=4)	−76.3 (n=2)	−89.8 (n=2)
4–6 years (n=11[c])	−82.0 (n=7)	−88.1 (n=8)	−83.3 (n=2)	NE (n=0)
>6 years (n=15)	−81.6 (n=13)	−84.0 (n=12)	−78.3 (n=10)	−78.0 (n=9)
All (N=36)	−84.6 (n=28)	−86.2 (n=24)	−78.7 (n=14)	−80.1 (n=11)

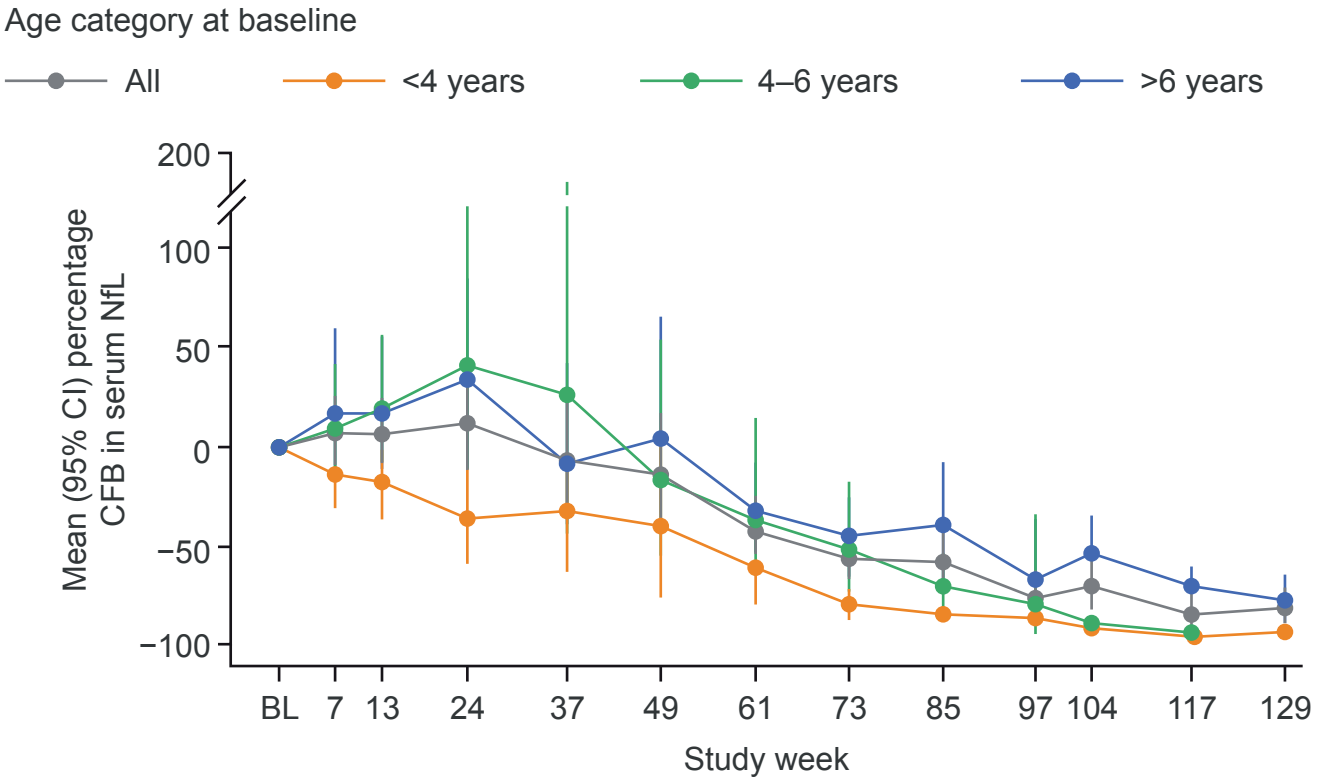


Age (n at baseline)	Mean CFB[d], %			
	Week 24	Week 49	Week 104	Week 129
<4 years (n=10)	−93.8 (n=8)	−94.6 (n=4)	−77.9 (n=2)	−95.9 (n=2)
4–6 years (n=11[c])	−88.1 (n=7)	−93.5 (n=8)	−90.5 (n=2)	NE (n=0)
>6 years (n=15)	−87.5 (n=13)	−88.5 (n=12)	−87.4 (n=10)	−89.7 (n=9)
All (N=36)	−89.5 (n=28)	−91.2 (n=24)	−86.5 (n=14)	−90.9 (n=11)



[a]Shaded gray area indicates the preliminary normal range of 1.61–3.6 µg/mg. [b]Shaded gray area indicates the preliminary normal range of 0.34–0.83 µg/mg. [c]Baseline value missing for one patient. [d]Data not shown for Week 153 because there were two participants in total. CFB, change from baseline; DS, dermatan sulfate; HS, heparan sulfate; MPS II, mucopolysaccharidosis type II; NE, not evaluable.

Supplemental Figure 3. Serum NfL mean percentage CFB



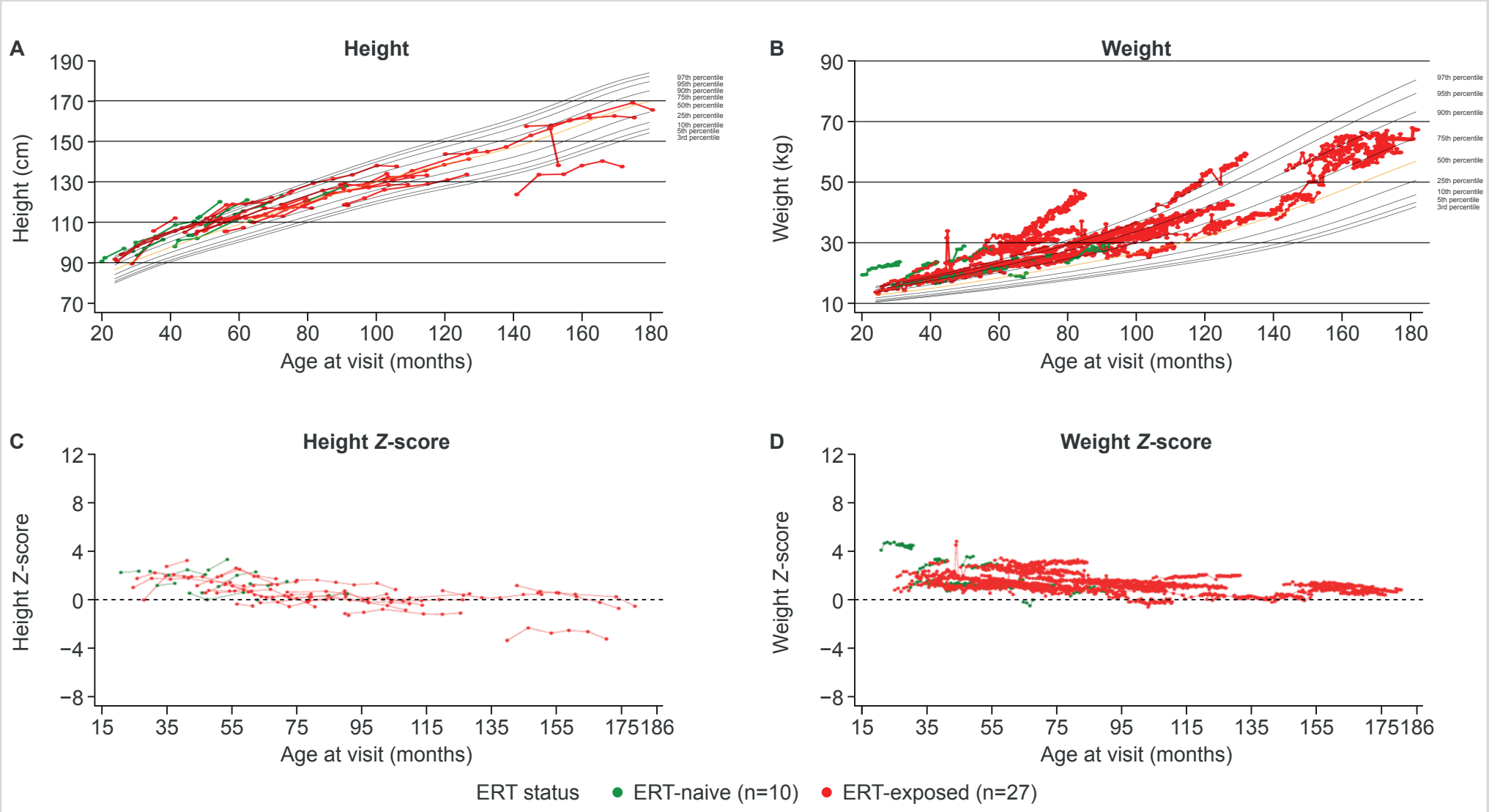
Number of participants, n

<4 years	7	6	7	7	6	5	6	5	3	3	2	3	2
4–6 years	8	8	8	8	7	7	7	7	5	4	3	2	0
>6 years	12	12	10	12	11	11	12	12	12	8	11	9	10
All	27	26	25	27	24	23	25	24	20	15	16	14	12

	Mean CFB, %					
Age	**Week 24**	**Week 37**	**Week 49**	**Week 61**	**Week 104**	**Week 129**
<4 years	−35.5	−31.7	−39.7	−59.8	−91.0	−92.7
4–6 years	40.4	26.4	−16.0	−36.4	−87.4	–
>6 years	32.8	−8.0	3.7	−31.8	−53.7*	−77.7*
All	11.9	−6.3	−13.5	−41.1*	−70.4*	−81.5*

**P*<0.001. Aggregate summaries by time point were provided for analysis visits that are common across all cohorts. The Week 7 analysis visit included observations closest to the target day (i.e. Day 43) from Weeks 5, 7 or 9. Mean CFB was computed from the geometric mean ratio relative to baseline. Corresponding 95% CI and *P* values were derived from the log ratio relative to baseline. Percentage CFB was derived as 100^{x-1}, in which x denotes the mean ratio, upper and lower limit for the mean ratio. BL, baseline; CFB, change from baseline; CI, confidence interval; NfL, neurofilament light chain.

Supplemental Figure 4. Individual participant (A) height, (B) weight, (C) height Z-score and (D) weight Z-score by age



ERT, enzyme replacement therapy.

REFERENCE

1. Hendriksz CJ *et al. Mol Genet Metab* Rep 2015;5:103–6.