CLAIMS

1. A nucleic acid construct comprising:
   (a) a nucleic acid sequence encoding a therapeutic protein, and
   (b) a nucleic acid sequence encoding a variant IGF2 (vIGF2) peptide having an amino acid sequence selected from SEQ ID NOs: 106, 107, 109, 111, 112, 113, 120 or 121.
2. The nucleic acid construct of claim 1, further comprising a sequence encoding a linker having a sequence that is at least 98% identical to a sequence selected from the group consisting of SEQ ID NOs: 181-188.
3. The nucleic acid construct of any one of claims 1 to 2, wherein the vIGF2 peptide is capable of increasing expression and/or secretion of a therapeutic protein compared to a vIGF2 peptide having the amino acid sequence of SEQ ID NO:80.
4. The nucleic acid construct of any one of claims 1 to 2, wherein the vIGF2 peptide has increased affinity for the CI-MPR as compared to a vIGF2 peptide having the amino acid sequence of SEQ ID NO:80.
5. The nucleic acid construct of claims 1 to 2, wherein the vIGF2 peptide is capable of improving uptake of the therapeutic protein into a cell.
6. The nucleic acid construct of any one of claims 1 to 5, wherein the therapeutic protein is capable of replacing a defective or deficient protein associated with a genetic disorder in a subject having the genetic disorder.
7. The nucleic acid construct of claim 6, wherein genetic disorder is a lysosomal storage disorder.
8. The nucleic acid construct of claim 6, wherein the genetic disorder is selected from the group consisting of aspartylglucosaminuria, CLN1/PPT1 disease, CLN2/TPP1 disease, cystinosis, Fabry disease, Gaucher disease type I, Gaucher disease type II, Gaucher disease type III, Pompe disease, Tay Sachs disease, Sandhoff disease, metachomatic leukodystrophy, mucolipidosis type I, mucolipidosis type II, mucolipidosis type III, mucolipidosis type IV, Hurler disease, Hunter disease, Sanfilippo disease type A, Sanfilippo disease type B, Sanfilippo disease type C, Sanfilippo disease type D, Morquio disease type A, Morquio disease type B, Maroteau-Lamy disease, Sly disease, Niemann-Pick disease type A, Niemann-Pick disease type B, Niemann-Pick disease type C1,

Niemann-Pick disease type C2, Schindler disease type I, Schindler disease type II, adenosine deaminase severe combined immunodeficiency (ADA-SCID), and neuronal ceroid lipofuscinosis.

9. The nucleic acid construct of claim 6 or claim 7, wherein the genetic disorder is selected from the group consisting of CLN1/PPT1 disease, CLN2/TPP1 disease, Pompe disease and MPS IIIB disease.

10. The nucleic acid construct of claim 9, wherein the genetic disorder is CLN1/PPT1 disease or CLN2/TPP1 disease.

11. The nucleic acid construct of any one of claims 1 to 10, wherein the therapeutic protein comprises a human enzyme selected from the group consisting of alpha-galactosidase (A or B), β-galactosidase, β-hexosaminidase (A or B), galactosylceramidase, arylsulfatase (A or B), β-glucocerebrosidase, glucocerebrosidase, lysosomal acid lipase, lysosomal enzyme acid sphingomyelinase, formylglycine-generating enzyme, iduronidase (e.g., alpha-L), acetyl-CoA:alpha-glucosaminide N-acetyltransferase, glycosaminoglycan alpha-L-iduronohydrolase, heparan N-sulfatase, N-acetyl-α-D-glucosaminidase (NAGLU), iduronate-2-sulfatase, galactosamine-6-sulfate sulfatase, N-acetylgalactosamine-6-sulfatase, N-sulfoglucosamine sulfohydrolase, glycosaminoglycan N–acetylgalactosamine 4-sulfatase, β-glucuronidase, hyaluronidase, alpha-N -acetyl neuraminidase (sialidase), ganglioside sialidase, phosphotransferase, alpha-glucosidase, alpha-D-mannosidase, beta-D-mannosidase, aspartylglucosaminidase, alpha-L-fucosidase, battenin, PPT1, TPP1, and other Batten-related proteins (e.g., ceroid-lipofuscinosis neuronal protein 6), or an enzymatically active fragment thereof.

12. The nucleic acid construct of claim 11, wherein the therapeutic protein is alpha-glucosidase, or an enzymatically active fragment thereof.

13. The nucleic acid construct of claim 11, wherein the therapeutic protein is human PPT1.

14. The nucleic acid construct of claim 11, wherein the therapeutic protein is human TPP1.

15. The nucleic acid construct of claim 11, wherein the therapeutic protein is human NAGLU.

16. The nucleic acid construct of claim 1, wherein the nucleic acid construct further comprises a sequence encoding a signal peptide.

17. The nucleic acid construct of claim 16, wherein the signal peptide is one of the sequences selected from the group consisting of SEQ ID NO:169-180.
18. The nucleic acid construct of any one of claims 1 to 17, wherein the vIGF2 encoding nucleic acid sequence is 5’ to the nucleic acid sequence encoding a therapeutic protein.
19. The nucleic acid construct of any one of claims 1 to 17, wherein the vIGF2 encoding nucleic acid sequence is 3’ to the nucleic acid sequence encoding a therapeutic protein.
20. A gene therapy vector comprising the nucleic acid construct of any one of claims 1 to 19.
21. The gene therapy vector of claim 20, wherein the gene therapy vector is a virus vector.
22. The gene therapy vector of claim 21, wherein the virus vector is an adenovirus vector, an adeno-associated virus (AAV) vector, a retrovirus vector, a lentivirus vector, a pox virus vector, a vaccinia virus vector, an adenovirus vector, or a herpes virus vector.
23. The nucleic acid construct of any one of claims 1 to 19, wherein the nucleic acid construct is a plasmid.
24. A pharmaceutical composition comprising a therapeutically effective amount of the nucleic acid construct of any one of claims 1 to 19 or 23 or the gene therapy vector of any one of claims 20 to 22, and a pharmaceutically acceptable carrier or excipient.
25. The pharmaceutical composition of claim 24, wherein the excipient comprises a non-ionic, low-osmolar compound, a buffer, a polymer, a salt, or a combination thereof.
26. Use of the nucleic acid construct of any one of claims 1 to 19 or 23 or the gene therapy vector of any one of claims 20 to 22 or the pharmaceutical composition of claim 24 or claim 25, in the manufacture of a medicament for the treatment of a genetic disorder.
27. The use of claim 26, wherein the genetic disorder is a lysosomal storage disorder.
28. The nucleic acid construct of any one of claims 1 to 19 or 23 or the gene therapy vector of any one of claims 20 to 22 or the pharmaceutical composition of claim 24 or claim 25, for use in therapy.