CLAIMS

1. A nucleic acid molecule encoding a functional chimeric GAA protein, comprising a signal peptide moiety and a functional human GAA moiety, in particular a functional human GAA moiety corresponding to a truncated form of a functional parent human GAA, wherein the signal peptide moiety has an amino acid sequence selected in the group consisting of SEQ ID NO:2 to 4, preferably SEQ ID NO:2,

or wherein the signal peptide moiety is a functional signal peptide moiety having an amino acid sequence comprising from 1 to 5, in particular from 1 to 4, in particular from 1 to 3, in particular from 1 to 2, in particular 1 amino acid deletion(s), insertion(s) or substitution(s) as compared to the sequence of SEQ ID NOs:2 to 4.

2. The nucleic acid molecule according to claim 1, wherein said functional human GAA moiety has 1 to 75 consecutive amino acids truncated at its N-terminal end as compared to a functional parent GAA polypeptide, wherein said functional human GAA moiety has in particular 6, 7, 8, 9, 10, 40, 41, 42, 43, 44, 45 or 46 consecutive amino acids truncated at its N-terminal end as compared to a functional parent human GAA polypeptide, in particular 8, 42 or 43 consecutive amino acids truncated at its N-terminal end as compared to a functional parent human GAA polypeptide.

3. The nucleic acid molecule according to any one of claims 1 to 2, wherein said functional human GAA moiety has 8 consecutive amino acids truncated at its N-terminal end as compared to a functional parent human GAA.

4. The nucleic acid molecule according to any one of claims 1 to 3, wherein said functional parent GAA is the human GAA polypeptide shown in SEQ ID NO:5 or SEQ ID NO:36, in particular SEQ ID NO:5.

5. The nucleic acid molecule according to any one of claims 1 to 4, which is a nucleotide sequence selected from the nucleotide sequence shown in SEQ ID NO:13 or 14.

6. The nucleic acid molecule according to any one of claims 1 to 5, comprising a nucleotide sequence resulting from the combination of the following sequences:

Signal peptide moiety coding sequence	GAA moiety coding sequence
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:31

SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:13
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:14
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:32
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:33
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:34
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:35
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:44
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:45
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:46
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:47
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:48
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:49

SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:50
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:51
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:52
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:53
SEQ ID NO:26 SEQ ID NO:27 SEQ ID NO:28	SEQ ID NO:54

7. A nucleic acid construct, comprising the nucleic acid molecule according to any one of claims 1 to 6, which is an expression cassette comprising said nucleic acid molecule operably linked to a promoter, such as a liver-specific promoter preferably selected in the group consisting of the alpha-1 antitrypsin promoter (hAAT), the transthyretin promoter, the albumin promoter and the thyroxine-binding globulin (TBG) promoter, wherein said nucleic acid construct optionally further comprises an intron, in particular an intron selected in the group consisting of a human beta globin b2 (or HBB2) intron, a FIX intron, a chicken beta-globin intron and a SV40 intron, wherein said intron is optionally a modified intron such as a modified HBB2 intron of SEQ ID NO:7, a modified FIX intron of SEQ ID NO:9, or a modified chicken beta-globin intron of SEQ ID NO:11.

8. The nucleic acid construct according to claim 7, comprising, preferably in this order,: an enhancer; an intron; a promoter, in particular a liver-specific promoter; the nucleic acid sequence encoding the chimeric GAA polypeptide; and a polyadenylation signal, the construct comprising preferably, in this order: an ApoE control region; a HBB2 intron, in particular a modified HBB2 intron; a hAAT promoter; the nucleic acid sequence encoding the chimeric GAA polypeptide; and a bovine growth hormone polyadenylation signal, said nucleic acid construct more particularly comprising the nucleotide sequence of SEQ ID NO:20, 21 or 22 or a nucleotide sequence resulting from any one of the combinations shown in claim 6.

9. A cell transformed with the nucleic acid molecule of any one of claims 1 to 6 or the nucleic acid construct of any one of claims 7 to 8, wherein the cell is in particular a liver cell or a muscle cell.

10. A chimeric GAA polypeptide, comprising a signal peptide moiety and a functional human GAA moiety, wherein the signal peptide moiety is selected in the group consisting of SEQ ID NO:2 to 4 or wherein the signal peptide moiety is a functional signal peptide moiety having an amino acid sequence comprising from 1 to 3, in particular from 1 to 2, in particular 1 amino acid deletion(s), insertion(s) or substitution(s) as compared to the sequence of SEQ ID NOs:2 to 4,

wherein in particular the functional human GAA moiety is a truncated form of a functional parent human GAA polypeptide, such as a functional human GAA moiety having 1 to 75 consecutive amino acids deleted at its N-terminal end as compared to a functional parent human GAA polypeptide, in particular 6, 7, 8, 9, 10, 20, 27, 28, 29, 30, 31, 41, 42, 43, 44, 45 or 45, more particularly 6, 7, 8, 9, 10, 20, 41, 42, 43 or 44 consecutive amino acids deleted at its N-terminal end as compared to a functional parent human GAA polypeptide, wherein the functional human GAA moiety is in particular a truncated form of the human GAA protein of SEQ ID NO:5 or SEQ ID NO:36, in particular of SEQ ID NO:5.

11. The chimeric GAA polypeptide according to claim 10, wherein the functional human GAA moiety has 8, 29, 42 or 43 consecutive amino acids truncated at its N-terminal end as compared to a functional parent human GAA polypeptide, more particularly 8 or 42, in particular 8, consecutive amino acids truncated at its N-terminal end as compared to a functional parent human GAA polypeptide, in particular as compared to the human GAA protein of SEQ ID NO:5 or SEQ ID NO:36, in particular of SEQ ID NO:5.

12. The chimeric GAA polypeptide according to claim 10 or 11, comprising an amino acid sequence resulting from the combination of the following sequences:

Signal peptide moiety	GAA moiety
SEQ ID NO:2 SEQ ID NO:3 SEQ ID NO:4	wild-type hGAA devoid of its natural signal peptide; e.g. SEQ ID NO:5 or SEQ ID NO:36, in particular SEQ ID NO:5
SEQ ID NO:2 SEQ ID NO:3 SEQ ID NO:4	truncated hGAA deleted for 8 consecutive N-terminal amino acids; e.g. SEQ ID NO:29
SEQ ID NO:2 SEQ ID NO:3 SEQ ID NO:4	truncated hGAA deleted for 29 consecutive N-terminal amino acids; e.g. SEQ ID NO:41

SEQ ID NO:2 SEQ ID NO:3 SEQ ID NO:4	Truncated hGAA deleted for 42 consecutive N-terminal amino acids; e.g. SEQ ID NO:30
SEQ ID NO:2 SEQ ID NO:3 SEQ ID NO:4	truncated hGAA deleted for 43 consecutive N-terminal amino acids; e.g. SEQ ID NO:42
SEQ ID NO:2 SEQ ID NO:3 SEQ ID NO:4	truncated hGAA deleted for 47 consecutive N-terminal amino acids; e.g. SEQ ID NO:43

13. A pharmaceutical composition, comprising, in a pharmaceutically acceptable carrier, the nucleic acid sequence of any one of claims 1 to 6, the nucleic acid construct of any one of claims 7 to 8, the cell according to claim 9, or the chimeric polypeptide according to any one of claims 10 to 12.

14. The nucleic acid sequence of any one of claims 1 to 6, the nucleic acid construct of any one of claims 7 to 8, the cell according to claim 9, or the chimeric polypeptide according to any one of claims 10 to 12, for use as a medicament.

15. Use of the nucleic acid sequence of any one of claims 1 to 6, the nucleic acid construct of any one of claims 7 to 8, the cell according to claim 9, or the chimeric polypeptide according to any one of claims 10 to 12, in the manufacture of a medicament for treating a glycogen storage disease, such as GSDI (von Gierke's disease), GSDII (Pompe disease), GSDIII (Cori disease), GSDIV, GSDV, GSDVI, GSDVII, GSDVIII and lethal congenital glycogen storage disease of the heart, more particularly GSDI, GSDII or GSDIII, even more particularly GSDII and GSDIII, and most particularly GSDII.