

Variant: *NM_000152.5(GAA):c.1847dup (p.Asp616fs)*

Version: 1.2

CA628018362 [↗](#)

693996 (ClinVar) [↗](#)

Gene: GAA ([HGNC:2548](#))

Condition: glycogen storage disease II ([MONDO:0009290](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: a6d35c95-71e2-47f1-902b-96063f067f0c

Approved on: 2026/4/9

Published on: 2026/4/9

HGVS expressions

NM_000152.5(GAA):c.1847dup (p.Asp616fs)

NM_000152.5:c.1847dup

NM_000152.5:c.1847dupA

NC_000017.11:g.80112670dup

CM000679.2:g.80112670dup

NC_000017.10:g.78086469dup

CM000679.1:g.78086469dup

NC_000017.9:g.75701064dup

NG_009822.1:g.16115dup

ENST00000570803.6:c.1847dup

ENST00000572080.2:c.1847dup

ENST00000577106.6:c.1847dup

ENST00000302262.8:c.1847dup

ENST00000302262.7:c.1847dup

ENST00000390015.7:c.1847dup

ENST00000570716.1:n.287dup

ENST00000572080.1:c.235dup

ENST00000572803.1:n.461dup

NM_000152.3:c.1847dup

NM_001079803.1:c.1847dup

NM_001079804.1:c.1847dup

NM_000152.4:c.1847dup

NM_001079803.2:c.1847dup

NM_001079804.2:c.1847dup

NM_001079803.3:c.1847dup

NM_001079804.3:c.1847dup

Likely Pathogenic

Met criteria codes **2**

PM2_Supporting

PVS1

Not Met criteria codes **2**

PP4

PM3

Evidence Links **0**

Expert Panel

Lysosomal Diseases VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Lysosomal Storage Disorders Variant Curation Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2

Evidence submitted by expert panel

Lysosomal Diseases VCEP

The NM_000152.5:c.1847dup (p.Asp616GlufsTer20) variant in GAA is a frameshift variant predicted to cause a premature stop codon in exon 14 out of a total of 20 exons, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). The highest population minor allele frequency in gnomAD v4.1.0. is 0.000003391 (4/1179640 alleles) in the European non-Finnish population, which is lower than the ClinGen LD VCEP's threshold (<0.001) for PM2_Supporting, meeting this criterion (PM2_Supporting). The variant was identified in a French patient with late onset Pompe disease (PMID 30155607). However, no clinical or laboratory information about the patient, such symptoms, residual GAA activity, or second variant, were provided (PM3_Not Met, PP4_Not Met). There is a ClinVar entry for this variant (Variation ID: 693996). In summary, this variant meets the criteria to be classified as likely pathogenic for Pompe disease. The classification of this variant has been upgraded from Variant of Uncertain Significance to Likely Pathogenic based on the recommendations of the ClinGen Sequence Variant Interpretation Working Group, that a variant meeting PVS1 and PM2_Supporting is classified as Likely Pathogenic (https://clinicalgenome.org/site/assets/files/5182/pm2_-_svi_recommendation_-_approved_sept2020.pdf) GAA-specific ACMG/AMP criteria applied, as specified by the ClinGen Lysosomal Diseases VCEP (Specifications Version 2.0): PVS1, PM2_Supporting. (Classification approved by the ClinGen Lysosomal Diseases VCEP on April 9, 2026)

Met criteria codes

PM2_Supporting	✓	The highest population minor allele frequency in gnomAD v4.1.0. is 0.000003391 (4/1179640 alleles) in the European non-Finnish population, which is lower than the ClinGen LD VCEP's threshold (<0.001) for PM2_Supporting, meeting this criterion.
PVS1	<div><div></div><div>✓</div></div>	The NM_000152.5:c.1847dup (p.Asp616GlufsTer20) variant in GAA is a frameshift variant predicted to cause a premature stop codon in exon 14 out of a total of 20 exons, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

Not Met criteria codes

PP4	<div><div></div><div>✗</div></div>	The variant was identified in a French patient with late onset Pompe disease (PMID 30155607). However, individual details about the patient, including residual GAA activity, were not provided. Therefore, PP4 is not currently met.
PM3	<div><div></div><div>✗</div></div>	The variant was identified in a French patient with late onset Pompe disease (PMID 30155607). However, individual details about the patient, including residual GAA activity and the second variant were not provided. Therefore, PM3 is not currently met.

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