c.460+1G_A — WFS1 Molecular Atlas Card

Variant type: Splice site

Boundary: donor (5' splice site) · intronic offset +1

Nearest protein position: ~154 (N-terminal cytoplasmic (intrinsically disordered))

SCHEMA CATEGORY: S2 — PREDICTED FRAMESHIFT SKIP OF EXON 4 (145 NT)

SpliceAI predicts strong donor (5') loss (ΔS 1.00) -> skipping of exon 4 (145 nt, NOT divisible by 3), which shifts the reading frame downstream. A premature stop is predicted at ~aa 115. The frameshifted/truncated product follows the frameshift schema (F1/F2 by NMD); typically too compromised for chaperone rescue — gene-therapy track. (acceptor-gain 0.00, acceptor-loss 0.00, donor-gain 0.96, donor-loss 1.00.)

SPLICE PREDICTION

- **Affected site:** donor (5' splice site), canonical (±1/±2 core)
- **SpliceAI delta scores** (GRCh38 chr4:6289132 G>A):

- acceptor gain **0.00** · acceptor loss **0.00**

- donor gain **0.96** · donor loss **1.00**

- **Predicted outcome:** Predicted frameshift skip of exon 4 (145 nt)

CLINICAL EVIDENCE

- **Classification:** Pathogenic
- **Review status:** criteria provided, multiple submitters, no conflicts
- **cDNA change:** c.460+1G>A
- **ClinVar accession:** VCV000004515

- **Last evaluated:** 2024/10/23 00:00
- **Submissions:** 1

Card generated by `wolfram-atlas-batch` (splice pipeline) on 2026-06-08T07:50:33.326616Z.

Schema: `reference/card` `schemaextension.md` (S1–S3). WFS1: UniProt O76024, AlphaFold v6.