The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000330.4(RS1):c.68C>A (p.Ser23Ter)

Version: 1.0

CA226850

99020 (ClinVar)

Gene: RS1 (HGNC:6247)
Condition: X-linked retinoschisis (MONDO:0010725)
Inheritance Mode: X-linked inheritance (recessive (HP:0001419))
UUID: 1d11041f-c842-43cf-aed8-bf2e2e346dc1
Approved on: 2025/5/19
Published on: 2025/5/20

HGVS expressions

NM_000330.4(RS1):c.68C>A (p.Ser23Ter)
NM_000330.4:c.68C>A
NC_000023.11:g.18657650G>T
CM000685.2:g.18657650G>T
NC_000023.10:g.18675770G>T
CM000685.1:g.18675770G>T
NC_000023.9:g.18585691G>T
NG_008659.3:g.24799C>A
ENST00000379984.4:c.68C>A
ENST00000379984.3:c.68C>A
NM_000330.3:c.68C>A

Pathogenic

Met criteria codes 3

PS4_Supporting PVS1 PM2_Supporting

Evidence Links 0

Expert Panel

X-linked Inherited Retinal Disease VCEP

Criteria Specification Information

Criteria Specification: *ClinGen X-linked Inherited Retinal Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RS1 Version 1.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

X-linked Inherited Retinal Disease VCEP

The NM_000330.4(RS1):c.68C>A variant is a nonsense variant in amino acid 23, which results in a premature stop codon and causes a truncated protein. This is a nonsense variant that introduces a premature stop codon between amino acids 1-223 that is predicted to either trigger nonsense-mediated decay or to disrupt a critical C-terminal region required for proper multimerization of RS1 (PVS1, PMID: 19849666). This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting). This variant has been reported in at least 2 probands meeting the PS4 requirement of a male diagnosed with X-linked retinoschisis (PS4_supporting, PMIDs: 9618178, 35456481). In summary, this variant is classified as pathogenic for X-linked retinoschisis based on the ClinGen X-linked Inherited Retinal

Disease Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RS1 Version 1.0.0: PVS1, PS4_supporting, and PM2_supporting (date of approval 01/24/2025).

Met criteria codes

PS4_Supporting	✔	This variant has been reported in at least 2 proband meeting the PS4 requirement of a male diagnosed with XLRS (PS4_supporting, PMIDs: 9618178, 35456481).
PVS1	✔	This is a nonsense variant that introduces a premature stop codon between amino acids 1-223 that is predicted to either trigger nonsense-mediated decay or to disrupt a critical C-terminal region required for proper multimerization of RS1 (PVS1, PMID: 19849666).
PM2_Supporting	✔	This variant is absent from hemizygous individuals in gnomAD v4.1.0 (PM2_Supporting).

Curation History

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