Solutions

2.1

- Nonsense (premature stop).

2.2

- Variant of uncertain significance – explicitly unknown.

2.3

- CNV (copy number variant).

3.1

- Likely pathogenic/pathogenic: truncation in a gene where one working copy is insufficient is loss-of-function disease.
- In a dominant-negative gene, missense (poison peptide) variants matter more than truncation.
- Severity tends to track the variant type and position – truncations early are often more severe.

3.2

- "We found a spelling change; we do not yet know if it means anything" – no cascade testing on a VUS. Upgrades: co-segregation with disease in the family; more affected carriers reported over time (and functional studies).
- Harm: unnecessary prophylactic surgery in relatives treated as carriers.