**Supplement 2**

**Other tiered variants in patient WES or WGS data**

**Patient 3** carried a heterozygous variant of unknown significance in *COL4A3* [NM\_000091.4:c.4981C>T, p.(Arg1661Cys)], which was maternally inherited. Pathogenic heterozygous variants in *COL4A3* cause autosomal dominant Alport syndrome (OMIM#104200).

**Patient 8** carried a homozygous variant of unknown significance in *PNPT1* [NM\_033109.4: c.493C>T, p.(Pro165Ser)]. Pathogenic variants in *PNPT1* cause autosomal recessive combined oxidative phosphorylation deficiency 13 (OMIM#61432).

Detailed further analysis of the WGS data from Patient 1 did not identify any further Tier 1-3 variants associated with other plausible phenotypes, including diseases that have been catalogued in the Irish Traveller population to date18 (see Supplemental Table 1).