HNF4A 9/15/2023

Nonsense or Frameshift	Exons 1-9 (5’ of c.1162) because NMD[b] is expected		PVS1
	Last 55 base pairs of exon 9 (c.1162 – c.1216) and first 41 base pairs of exon 10 (c. 1217 – c.1257) because known MODY nonsense/frameshift variants occur at and 5’ of corresponding aa Ser419		PVS1
	Exon 10 3’ of c.1257 (Gly420)		PVS1_Supporting
GT--AG 1,2 splice sites [a]	Skipping of exon 1, 2, 3, 4, or 6 or use of a cryptic splice site results in frameshift that causes PTC 5’ of c.1257/Ser419		PVS1
	Skipping of exon 5, 7, 8, or 9 (preserves reading frame but removes >10% of protein)		PVS1_Strong
	Skipping of or stop loss in exon 10 (removes transactivation domain)[c]		PVS1_Strong
Deletion (Single exon to full gene)	Full gene deletion[d]		PVS1
	Single to multi exon deletion – exons 1, 2, 3, 4, or 6		PVS1
	Single exon deletion: exon 5, 7, 8, or 9, or 10		PVS1_Strong
Duplication (≥1 exon in size and must be completely contained within gene)	Proven in tandem	Reading frame disrupted and NMD predicted to occur	PVS1
		No or unknown impact on reading frame and NMD	N/A
	Presumed in tandem	Reading frame disrupted and NMD predicted to occur	PVS1_Strong
		No or unknown impact on reading frame and NMD	N/A
	Proven not in tandem		N/A
Initiation Codon			PVS1_Strong