Supplementary Table 1

Predisposing variants in SMAD4

| Family nr. | Variant | Classification | Exon number | Type               |
|------------|---------|----------------|-------------|--------------------|
| I          | c.1156G>A | p.(Gly386Ser)  | Likely pathogenic | Exon 10 | Missense          |
| II         | t(1;18)(p36.1;q21.1) |                  |             | Chromosomal translocation |
| III        | c.723_730del | p.(Gly243Alafs*18) | Pathogenic | Exon 6 | Frameshift        |
| IV         | c.1325_1326del | p.(Gln442Leufs*51) | Pathogenic | Exon 11 | Frameshift        |
| V          | c.1245_1248del | p.(Asp415Glufs*20) | Pathogenic | Exon 10 | Frameshift        |
| VI         | c.1421del | p.(Ser474Ter) | Pathogenic | Exon 11 | Nonsense          |
| VII        | del (c.955+1_956-1)_(_1308+1_1309-1)del | p.(Ala319Glyfs*3) | Pathogenic | Exon 9-10 | Frameshift        |
| VIII       | c.330dupA | p.(His111Thrfs*3) | Pathogenic | Exon 3 | Frameshift        |
| IX         | c.1081C>T | p.(Arg361Cys) | Pathogenic | Exon 9 | Missense          |
| X          | c.1245_1248del | p.(Asp415Glufs*20) | Pathogenic | Exon 10 | Frameshift        |
| XI         | c.1587dup | p.(His530Thrfs*47) | Pathogenic | Exon 12 | Frameshift        |
| XII        | c.939del | p.(Ile314Phefs*22) | Pathogenic | Exon 8 | Frameshift        |
| XIII       | c.692dup | p.(Ser232Glufs*3) | Pathogenic | Exon 6 | Frameshift        |
| XIV        | c.1448-1G>A | p.? | Likely pathogenic | Intron 11 | Splice site       |
| XV         | c.831_832del | p.(Pro278Ter) | Pathogenic | Exon 7 | Nonsense          |

1. NM_005359.5
2. According to ACMG standards and guidelines (Richards et al. 2015)