

Supplementary Materials S1: Sequences of splice products obtained in the minigene splice assay of the *SMO* c.1264+3G>C variant

WT normal 2 (425bp)- normal splicing product

WT upper band 5 (791bp)- abnormal splicing product (intron 5+6 retention)

WT upper band 4 (464bp)- abnormal splicing product (partial intron 5 retention)

WT upper band 17 (700bp)- abnormal splicing product (intron 5 retention)

Var1 normal (425bp)- normal splicing product

Var1 upper band 10 (791bp)- abnormal splicing product (intron 5+6 retention)

Var1 12 (301bp)- abnormal splicing product (skipping of exon 6)

Var1 9 (150bp)- abnormal splicing product (uses splice sites within exons 5 and 6)

Var1 upper band 11 (452bp)- abnormal splicing product (partial intron 5 retention)

WT normal 2 (425bp)- normal splicing product

GCCATGGCGGCCGCGGGNATTGATTGATATCGCATGGTCTCGTTGATCTTGCT
GGCAGCCTTCTCACTCAGCAGCCCCGGGGTGGTTGCTCTTGATGGAGAACAGAGTC
ATGACTCCTCGGATGAGGAAGCAGCCTCCACGATGAGCACCAGGCCGATTGGGG
CCAGCACGAAGCCCGCACGGTATCGGTAGTTCTTGAGCCCACAAAACAA
ATGCCACTCACAGAGTCCCCATCCACCTGCGCCACAGCAAGGATTACCACAGTGG
GACAAAGGGGAGTGACCAGGTGAGCAGGTGGAAGTAGGAGGTCTTGCCCGAGAGA
GGCTGGTAGGTGGTGCCAGGGCTTTGAAGGAAGTGTGCCAGGCATAGG
TGAGGACCACAAACCAAACACACCAGCCATCAGGGCGTAGTACACGATGACAAA
GATGATGACGCAGGACAGAGTCTCATTGGAGCTCAATCACTAGTGAATTCGCGGCC
GCCTGCAGGTCGACCATATGGGAGAGCTCCCAACGCGTTGGATGCATAG
CTTGAGTATTCTATAGTGTCACCTAAATAGCTTGCGTAATCATGGTCATAGCTGTTTCC
TGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAG
TGTAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTA
ATTGCGTTGCGCTCACTGCCCCGCTTTCAGTCGGGAAACCTGTCGTGCCAGCTGCA
TTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCC
GCTTCCTCGCTCACTGACTCGCTGCGCTCGGTTCGGCTGCGGCGAG
CGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCNGGGGATAAC
GCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAGGCCAGGAACCGTAAAAAGG
CCGCGTTGCTGGCGTTTTTCCAT

WT upper band 5 (791bp)- abnormal splicing product (intron 5+6 retention)

TGGCGGCCGCGGGAATTCGATTGAGCTCCAATGAGACTCTGTCCTG
CGTCATCATCTTTGTCATCGTGTACTACGCCCTGATGGCTGGTGTGGTTTGGTTTGTGG
TCCTCACCTATGCCTGGCACACTTCCTTCAAAGCCCTGGGCACCACCTACCAGCCT
CTCTCGGGCAAGACCTCCTACTTCCACCTGCTCACCTGGTCACTC
CCCTTTGTCCTCACTGTGGCAATCCTTGCTGTGGCGCAGGTATAGTGAAGTGGTAGGA
ACGGGAGACCTGGATGGGGTGAGTTTGAGGGAGGGGGCCAGTAACCCACCTTCTG
TCCCACCCCTTCCTGCTGCAGGTGGATGGGGACTCTGTGAGTGGCATT
TGTTTTGTGGGCTACAAGAACTACCGATAACCGTGCGGGCTTCGTGCTGGCCCCAAT
CGGCCTGGTGCTTATCGTGGGAGGCTACTTCCTCATCCGAGGTGAGTGAAGACCAG
GCTAGGACCAGTTGGGCAACAAAATGTACTGGGCACTTGCTGCCAGTA
CTGGGAGCTGCCAGCACGGCTGCCCCCATGCTGAAACCCAGCTAGCTCCTAGG
ATCCCCATTTCTCCAGTGTCTCTAGCTCCCCAGGTTTTTCATTAGCACAGGGGTAATC
AGACTTGGGACTCCAGAGCCTTANGACCCTCCTCCCACTCACCCATCC
TTCCCAGCGGGGCAGCCTCACCCCTGCTAATGTCTGAGGTCCCCCTTCTGTTTCANG
AGTCATGACTCTGTTCTCCATCAAGAGCAACCACCCCGGGCTGCTGAGTGAGAAGG
CTGCCAGCAAGATCAACGAGACCATGCGATATCAATCACTAGTGAATT
CGCGGGCCGCTGCAGGTCGACCATATGGGAGAGCTNCCAACGCGTTGGATGCA
TAGCTTGAGTATTCTATAGTGTACCTAAATAGCTTGGGCGTAATCATGG

WT upper band 4 (464bp)- abnormal splicing product (partial intron 5 retention)

ATGGCGGCCGCGGGNATTCGATTGAGCTCCAATGAGACTCTGTCCTGCG
TCATCATCTTTGTCATCGTGTACTACGCCCTGATGGCTGGTGTGGTTTGGTTTGTGGTC
CTCACCTATGCCTGGCACACTTCCTTCAAAGCCCTGGGCACCACCTACCAGCCTCT
CTCGGGCAAGACCTCCTACTTCCACCTGCTCACCTGGTCACTCCC
CTTTGTCCTCACTGTGGCAATCCTTGCTGTGGCGCAGGTATAGTGACTGGTAGGAAC
GGGAGACCTGGATGGGGTGAGTTCGAGGGAGGGGGGCCAGTAACCCACCTTCTGTC
CCACCCCTTCCTGCTGCAGGTGGATGGGGACCCTGTGAGTGGCATTG
TTTTGTGGGCTACAAGAACTACCGATACCGTGCGGGCTTCGTGCTGGCCCCAATCG
GCCTGGTGCTCATCGTGGGAGGCTACTTCCTCATCCGAGGAGTCATGACTCTGTTCT
CCATCAAGAGCAACCACCCCGGGCTGCTGAGTGAGAAGGCTGCCAGC
AAGATCAACGAGACCATGCGATATCAATCACTAGTGAATTCGCGGGCCGCCTGCAGG
TCGACCATATGGGAGAGCTCCCAACGCGTTGGATGCATAGCTTGAGTATTCTATAGTG
TCACCTAAATAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTG
TGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTA
AAGCCTGGGGTGCTAATGAGTGAGCTAACTCACATTAAATTGCGTTGCGCTCACTGC
CCGCTTTCAGTCGGGAAACCTGTGCTGCCAGCTGCATTAATGAA
TCGGGCCAACGCGCGGGGAGAGGCGGTTTGCATTGGGCGCTCTTCCGCTTCCT
CGCTCACTGACTCGCTGCGCTCGGTGCTTCGGCTGCGGCGAGCGGTATCAGCTCA
CTCAAAAGC

WT upper band 17 (700bp)- abnormal splicing product (intron 5 retention)

ATTCGATTGATATCGCATGGTCTCGTTGATCTTGCTGG
CAGCCTTCTCACTCAGCAGCCCGGGTGGTTGCTCTTGATGGAGAACAGAGTCATG
ACTCCTGAACAGAAGGGGGACCTCAGACATTAGCAGGGGTGAGGCTGCCCTGCTG
GGAAGGATGGGTGAGTGGGAGGAGGGTCCTAAGGCTCTGGAGTCCCAAG
TCTGATTACCCCTGTGCTAAATGAAAACCTGGGGAGCTAGAGACACTGGAGAAATGG
GGATCCTAGGAGCTAGCTGGGGTTTCAGCATGGGGGCAGCCGTGCTGGCAGCTCC
CAGTACTGGCAGCAAGTGCCCAGTACATTTTGTGCCCCAACTGGTCCT
AGCCTGGTCTTCACTCACCTCGGATGAGGAAGTAGCCTCCCACGATGAGCACCAG
GCCGACTGGGGCCAGCACGAAGCCCGCACGGTATCGGTAGTTCTTGTAGCCCACA
AAACAAATGCCACTCACAGAGTCCCCATCCACCTGCGCCACAGCAGGGAT
TGCCACAGTGAGGACAAAGGGGAGTGACCAGGTGAGCAGGTGGAAGTAGGAGGTC
TTGCCCCGAGAGAGGCTGGTAGGTGGTGCCAGGGCTTTGAAGGAAGTGTGCCAGG
CATAGGTGAGGACCACAAACCAACACACCAGCCATCAGGGCGTAGTAC
ACGATGACAAAGATGATGACGCANGACAGAGTCTCATTGGAGCTCAATCACTAGTGA
ATTCGCGGNCGCCTGCAGGTGCACCATATGGGAGAGCTCCCNACGCGTTGGATGC
ATAGCTTGAGTATTCTATAGTGTACCTAAATAGCTTGGCGTAATCAT
GGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCNCATTTCCACACAACATACGA
GCCGGAAGCNNNAAAGTGNA
AGCCTGGGGNGCCTAATGAGTGAGCTTAC

Var1 normal (425bp)- normal splicing product

ATGGCGGCCGCGGGAATTCGATTGATATCGCATGGTCTCGTTGAT
CTTGCTGGCAGCCTTCTCACTCAGCAGCCCCGGGTGGTTGCTCTTGATGGAGAACA
GAGTCATGACTCCTCGGATGAGGAAGTAGCCTCCCACGATGAGCACCAGGCCGATT
GGGGCCAGCACGAAGCCCGCACGGTATCGGTAGTTCTTGTAAGCCACA
AAACAAATGCCACTCACAGAGTCCCCATCCACCTGCGCCACAGCAAGGATTGCCA
CAGTGAGGACAAAGGGGAGTGACCAGGTGAGCAGGTGGAAGTAGGAGGTCTTGCC
CGAGAGAGGCTGGTAGGTGGTGCCAGGGCTTTGAAGGAAGTGTGCCAGG
CATAGGTGAGGACCACAAACCAACACACCAGCCATCAGGGCGTAGTACACGAT
GACAAAGATGATGACGCAGGACAGAGTCTCATTGGAGCTCAATCACTAGTGAATTG
CGGCCGCCTGCAGGTGACCATATGGGAGAGCTCCCAACGCGTTGGAT
GCATAGCTTGAGTATTCTATAGTGTCACCTAAATAGCTTGGCGTAATCATGGTCATAGCT
GTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGC
ATAAAGTGTAAGCCTGGGGTGCCCTAATGAGTGAGCTAACTC
ACATTAATTGCGTTGCGCTCACTGCCCCGCTTTCCAGTCGGGAAACCTGTCTGTGCCA
GCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGC
TCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCTGTTCCGGCTGC
GGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGG
GATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCAGGAACCGTAA
AAAGGCCGCGTTGCTGGCGNTTTTNCATAA

Var1 upper band 10 (791bp)- abnormal splicing product (intron 5+6 retention)

CGCCATGGCGGCCGCGGGAATTCGATTGAGCTCCAATGAGACTCTGTCCTGCG
TCACCATCTTTGTCATCGTGTACTACGCCCTGATGGCTGGTGTGGTTTGGTTTGTGGTC
CTCACCTATGCCTGGCACACTTCCTTCAAAGCCCTGGGCACCACCTACCAGCCTCT
CTCGGGCAAGACCTCCTACTTCCACCTGCTCACCTGGTCACTCCC
CTTTGTCCTCACTGTGGCAATCCTTGCTGTGGCGCAGGTATAGTGACTGGTAGGAAC
GGGAGACCTGGGTGGGGTGAGTTTGAGGGAGGGGGGCCAGTAACCCACCTTCTGTC
CCACCCCTTCCTGCTGCAGGTGGATGGGGACTCTGTGAGTGGCATTG
TTTTGTGGGCTACAAGAACTACCGATACCGTGCGGGCTTCGTGCTGGCCCCAATCG
GCCTGGTGCTCACCGTGGGAGGCTACTTCCTCATCCGAGGTCAGTGAAGACCAGG
CCAGGACCAGTTGGGTAACAAAATGTACTGGGCACTTGCTGCCAGTACT
GGGAGCTGCCAGCACGGCTGCCCCCATGCTGAAACCCCAGCTAGCTCCTAGGAT
CCCCATTTCTCCAGTGTCTCTAGCTCCCCAGGTTTTTCATTAGCACAGGGGTAATCAG
ACTTGGGACTCCAGAGCCTTAGGACCCTCCTCCCACTCACCCATCCTT
CCCAGCAGGGCAGCCTCACCCCTGCTAATGTCTGAGGTCCCCCTTCTGTTTCAGGA
GTCATGACTCTGTTCTCCATCAAGAGCAACCACCCCGGGCTGCTGAGTGAGAAGGC
TGCCAGCAAGATCAACGAGACCATGCGATATCAATCACTAGTGAATTG
CGGCCGCCTGCAGGTGCACCATATGGGAGAGCTCCCAACGCGTTGGATGCATAGC
TTGAGTATTCTATAGTGTACCTAAATAGCTTGGCGTAATCATGGGTCATAGCTGTTTCC
TGTGTGAAATTGTTATCCGCTCACAATTCCNNNCAACATACGAGC
CGGAAGCATAAAGTGTAAGCCTGGGGNGCCCTAATGAGTGAGCTAACTCACCNNTT
AATTGCGTTTGCNCNTCACTGCCC
GCTTTCANTCGGAAAACCT

Var1 12 (301bp)- abnormal splicing product (skipping of exon 6)

TGGCGGCCGCGGGAATTCGATTGATATCGCATGGTCTCGTTGATCTTGCT
GGCAGCCTTCTCACTCAGCAGCCCCGGGGTGGTTGCTCTTGATGGAGAACAGAGTC
ATGACTCCTGCGCCACAGCAAGGATTGCCACAGTGAGGACAAAGGGGAGTGACCA
GGTGAGCAGGTGGAAGTAGGAGGTCTTGCCCCGAGAGAGGCTGGTAGGTGG
TGCCCAGGGCTTTGAAGGAAGTGTGCCAGGCATAGGTGAGGACCACAAACCAAAC
CACACCAGCCATCAGGGCGTAGTACACGATGACAAAGATGATGACGCAGGACAGA
GTCTCATTGGAGCTCAATCACTAGTGAATTCGCGGCCCGCCTGCAGGTCTGA
CCATATGGGAGAGCTCCCAACGCGTTGGATGCATAGCTTGAGTATTCTATAGTGTAC
CTAAATAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTC
ACAATTCCACACAACATACGAGCCGGAAGCATAAAGTGTA
GCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCC
GCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGC
GGGGAGAGGCGGTTTGCGTATTGGGCGCTCTTCGCTTCCTCGCTCA
CTGACTCGCTGCGCTCGGTCTGTCGGCTGCGGCGAGCGGTATCAGCTCACTCAA
GGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAG
CAAAGGCCAGCAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGC
GTTTTCCATNNCTCCGCCCCCTGACGAGCATCACAAAATCGACGCTCAAGTCA
GAGGTGGCGAAACCCGACAGGACTATAAGATACCAGGCGTTCCCCCTGGAAAG
CTCCCTCGNGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGGATACCT
GTCCGCCTTTCTCCCTTCGGGGAAGCG

Var1 9 (150bp)- abnormal splicing product (uses splice sites within exons 5 and 6)

TCCCGGCCGCCATGGCGGCCGCGGGAATTCGATTGAGCTCCAATGAGACTCTGTC
CTGCGTCATCATCTTTGTCATCGTGGGAGGCTACTTCCTCATCCGAGGAGTCATGACT
CTGTTCTCCATCAAGAGCAACCACCCCGGGCTGCTGAGTGAGAAGGCTGCCAGCA
AGATCAACGAGACCATGCGATATCAATCACTAGTGAATTCGCGGCCGCC
TGCAGGTCGACCATATGGGAGAGCTCCCAACGCGTTGGATGCATAGCTTGAGTATTC
TATAGTGTCACCTAAATAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATT
GTTATCCGCTCACAATTCCACACAACATACGAGCCGGAAGCAT
AAAGTGTAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCG
CTCACTGCCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCG
GCCAACGCGCGGGGAGAGGCGGTTTGGCGTATTGGGCGCTCTTCCGCT
TCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCCGGCTGCGGCGAGCGGTATCAG
CTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAG
AACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCG
CGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAATCGA
CGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCC
CCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTAC
CGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCAC
GCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTGCTCCAAGCTGGGCTGTGTGCACG
AACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGGTAAGTATCG
TCTTGAGTCCAACCCGGTAAGACAC

Var1 upper band 11 (452bp)- abnormal splicing product (partial intron 5 retention)

CCGCCATGGCGGCCGCGGGGAATTCGATTGATATCGCATGGTCTCGTTGATCTTGC
TGGCAGCCTTCTCACTCAGCAGCCCGGGGTGGTTGCTCTTGATGGAGAACAGAGTC
ATGACTCAGAGTCCCCATCCACCTGCGCCACAGCAAGGATTGCCACAGTGAGGAC
AAAGGGGAGTGACCAGGTGAGCAGGTGGAAGTAGGAGGTCTTGCCCGAG
AGAGGCCGGTAGGTGGTGCCCAAGGCTTTGAAGGAAGTGTGCCAGGCATAGGTGA
GGACCACAAACCAAACACACCAGCCATCAGGGCGTAGTACACGATGACAAAGAT
GATGACGCAGGACAGAGTCTCATTGGAGCTCAATCACTAGTGAATTCGCG
GCCGCCTGCAGGTGACCATATGGGAGAGCTCCCAACGCGTTGGATGCATAGCTT
GAGTATTCTATAGTGTACCTAAATAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGT
GTGAAATTGTTATCCGCTCACAAATTCCACACAACATACGAGCCGG
AAGCATAAAGTGTAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCG
TTGCGCTCACTGCCCGCTTTCCAGTCGGGAAACCTGTCGTGCCAGCTGCATTAATG
AATCGGCCAACGCGCGGGGAGAGGCGGTTTTCGTATTGGGCGCTCT
TCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCCGGCTGCGGCGAGCG
GTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCA
GGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGGCCAGGAACCGTAAA
AAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACA
AAAATCGACGCTCAAGTCAGAGGNGNCGAAACCCGACAGGACTATAAAGATACCA
GGCGTTTCCCCTGGAAGCTCCCTCGTGCGCTCTCCTNNTTCCGACCCTGC
GCTTACCGGATACCTGTC