iClust 1: N = 140 iClust 2: N = 72 SMAD3|ILMN\_1682738 (ER binding) SMAD3|ILMN\_1682738 (ER binding) [<=60] p = 0.82099No detectable trend: [<=60] p = 0.3594No detectable trend: 16 16 [>60] p = 0.41002 [>60] p = 0.025533|FC|<4 or adjPval>0.01 |FC|<4 or adjPval>0.01 [AII] p = 0.017512[AII] p = 0.0143424 4 Raw Expression (4, 16) Raw Expression (4, 16) 12 12 10 10 ω ω 9 9 20 40 60 80 100 20 40 60 80 100 Age at diagnosis Age at diagnosis iClust 3: N = 294 iClust 4: N = 344 SMAD3|ILMN\_1682738 (ER binding) SMAD3|ILMN\_1682738 (ER binding) [<=60] p = 0.95851No detectable trend: [<=60] p = 0.51563No detectable trend: 16 16 [>60] p = 0.0072863 |FC|<4 or adjPval>0.01 [>60] p = 0.57835|FC|<4 or adjPval>0.01 [AII] p = 0.52656[AII] p = 0.900914 4 Raw Expression (4, 16) Raw Expression (4, 16) 12 12 10 10 ω ω 9 9 20 40 60 80 100 20 40 60 80 100 Age at diagnosis Age at diagnosis

iClust 5: N = 191 iClust 6: N = 86 SMAD3|ILMN\_1682738 (ER binding) SMAD3|ILMN\_1682738 (ER binding) [<=60] p = 0.11801No detectable trend: [<=60] p = 0.33786No detectable trend: 16 16 [>60] p = 0.3605[>60] p = 0.62943|FC|<4 or adjPval>0.01 |FC|<4 or adjPval>0.01 [AII] p = 0.84359[AII] p = 0.959644 4 Raw Expression (4, 16) Raw Expression (4, 16) 12 12 10 10 ω ω 9 9 20 40 60 80 100 20 40 60 80 100 Age at diagnosis Age at diagnosis iClust 7: N = 193 iClust 8: N = 300 SMAD3|ILMN\_1682738 (ER binding) SMAD3|ILMN\_1682738 (ER binding) [<=60] p = 0.045412No detectable trend: [<=60] p = 0.14553No detectable trend: 16 16 [>60] p = 0.57494 |FC|<4 or adjPval>0.01 [>60] p = 0.29596 |FC|<4 or adjPval>0.01 [AII] p = 0.0046523[AII] p = 0.370054 4 Raw Expression (4, 16) Raw Expression (4, 16) 12 12 10 10 ω ω 9 9 20 40 60 80 100 20 40 60 80 100 Age at diagnosis Age at diagnosis

iClust 9: N = 146 SMAD3|ILMN\_1682738 (ER binding)

iClust 10: N = 226 SMAD3|ILMN\_1682738 (ER binding)

