

SEQUENCE LISTING

<110> F. Hoffmann-La Roche AG
NanoString Technologies, Inc.

<120> Obinutuzumab treatment of novel DLBCL patient subgroup

<130> AA1470 PCT S3

<150> US62/542,489

<151> 2017-08-08

<160> 14

<170> BiSSAP 1.3

<210> 1

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> The heavy chain variable region of obinutuzumab; mouse-human
chimeric polypeptide

<400> 1

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Tyr Ser

20 25 30

Trp Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

35 40 45

Gly Arg Ile Phe Pro Gly Asp Gly Asp Thr Asp Tyr Asn Gly Lys Phe

50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr

65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys

85 90 95

Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly

100 105 110

Thr Leu Val Thr Val Ser Ser

115

<210> 2

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> The KV1 light chain variable region of obinutuzumab; mouse-human chimeric polypeptide

<400> 2

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Leu His Ser
20 25 30
Asn Gly Ile Thr Tyr Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Gln Met Ser Asn Leu Val Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ala Gln Asn
85 90 95
Leu Glu Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110
Arg Thr Val
115

<210> 3

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> Nucleic acid sequence encoding the heavy chain variable region of obinutuzumab; mouse-human chimeric DNA

<400> 3

caggtgcaat tgggtcagtc tggcgctgaa gttaagaagc ctgggagttc agtgaaggtc 60

tcctgcaagg ctccggata cgccttcagc tattcttgga tcaattgggt gcggcaggcg 120

cctggacaag ggctcgagtg gatgggacgg atctttcccg gcgatgggga tactgactac 180

aatgggaaat tcaagggcag agtcacaatt accgccgaca aatccactag cacagcctat 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc aagaaatgtc 300

tttgatggtt actggcttgt ttactggggc cagggaaccc tggtcaccgt ctctca 357

<210> 4

<211> 345

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence encoding the KV1 light chain variable region of obinutuzumab; mouse-human chimeric DNA

<400> 4

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attagctgca ggtctagcaa gagcctcttg cacagcaatg gcatcactta tttgtattgg    120
tacctgcaaa agccagggca gtctccacag ctctgattt atcaaatgtc caaccttgct    180
tctggcgtcc ctgaccggtt ctccgatcc gggtcaggca ctgatttcac actgaaaatc    240
agcagggtgg aggctgagga tgttgaggtt tattactgcg ctgagaatct agaacttcct    300
tacaccttcg gcggaggggac caaggtggag atcaaacgta cgggtg                    345
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<210> 5

<211> 449

<212> PRT

<213> Artificial Sequence

<220>

<223> the heavy chain of obinutuzumab

<400> 5

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1      5      10      15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Tyr Ser
20     25     30
Trp Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35     40     45
Gly Arg Ile Phe Pro Gly Asp Gly Asp Thr Asp Tyr Asn Gly Lys Phe
50     55     60
Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65     70     75     80
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85     90     95
Ala Arg Asn Val Phe Asp Gly Tyr Trp Leu Val Tyr Trp Gly Gln Gly
100    105    110
Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
115    120    125
Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
130    135    140
Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
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145 150 155 160
 Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
 165 170 175
 Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
 180 185 190
 Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
 195 200 205
 Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys
 210 215 220
 Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
 225 230 235 240
 Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
 245 250 255
 Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
 260 265 270
 Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
 275 280 285
 Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
 290 295 300
 Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
 305 310 315 320
 Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
 325 330 335
 Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
 340 345 350
 Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr
 355 360 365
 Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
 370 375 380
 Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
 385 390 395 400
 Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
 405 410 415
 Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
 420 425 430
 Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
 435 440 445
 Lys

<210> 6

<211> 219

<212> PRT

<213> Artificial Sequence

<220>

<223> the KV1 light chain of obinutuzumab

<400> 6

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly

1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Leu His Ser

20 25 30

Asn Gly Ile Thr Tyr Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Ser

35 40 45

Pro Gln Leu Leu Ile Tyr Gln Met Ser Asn Leu Val Ser Gly Val Pro

50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile

65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ala Gln Asn

85 90 95

Leu Glu Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys

100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu

115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe

130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln

145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser

165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu

180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser

195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

210 215

<210> 7

<211> 357

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence encoding the heavy chain variable region of
obinutuzumab (B-HH6)

<400> 7

caggtgcaat tgggtgcagtc tggcgctgaa gttaagaagc ctgggagttc agtgaaggtc 60

tcctgcaagg cttccggata cgccttcagc tattcttgga tcaattgggt gcggcaggcg 120

cctggacaag ggctcgagtg gatgggacgg atctttcccg gcgatgggga tactgactac 180

aatgggaaat tcaagggcag agtcacaatt accgccgaca aatccactag cacagcctat 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc aagaaatgc 300

tttgatgggtt actggcttgt ttactggggc caggggaacc tggtcaccgt ctcctca 357

<210> 8

<211> 345

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence encoding the KV1 light chain variable region of obinutuzumab

<400> 8

gataatcgtga tgaccagac tccactctcc ctgcccgtca cccctggaga gcccgccagc 60

attagctgca ggtctagcaa gacaccttg cacagcaatg gcatcactta ttgtattgg 120

tacctgcaaa agccagggca gtctccacag ctctgattt atcaaatgtc caacctgtc 180

tctggcgtcc ctgaccggtt ctccgatcc gggtcaggca ctgattcac actgaaaatc 240

agcaggggtgg aggctgagga tgttgaggtt tattactgcg ctcagaatct agaacttct 300

tacaccttcg gcggaggag caaggtggag atcaaacgta cgggtg 345

<210> 9

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> the heavy chain of rituximab

<400> 9

Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

20 25 30

Asn Met His Trp Val Lys Gln Thr Pro Gly Arg Gly Leu Glu Trp Ile

35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe

50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr

65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys

85 90 95
 Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn Val Trp Gly
 100 105 110
 Ala Gly Thr Thr Val Thr Val Ser Ala Ala Ser Thr Lys Gly Pro Ser
 115 120 125
 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
 130 135 140
 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
 145 150 155 160
 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
 165 170 175
 Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
 180 185 190
 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
 195 200 205
 Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Ala Glu Pro Lys Ser Cys
 210 215 220
 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 225 230 235 240
 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
 245 250 255
 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 260 265 270
 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 275 280 285
 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
 290 295 300
 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 305 310 315 320
 Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 325 330 335
 Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 340 345 350
 Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
 355 360 365
 Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
 370 375 380
 Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
 385 390 395 400
 Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
 405 410 415
 Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
 420 425 430
 His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 435 440 445
 Pro Gly Lys
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<210> 10
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<223> the light chain of rituximab

<400> 10
Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 5 10 15
Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Ile
20 25 30
His Trp Phe Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
50 55 60
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65 70 75 80
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Ser Asn Pro Pro Thr
85 90 95
Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205
Asn Arg Gly Glu Cys
210

<210> 11
<211> 1153
<212> DNA
<213> Homo sapiens

<400> 11
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catggttgct gggagcgacg cggggcgggc cctgggggtc ctcagcgtgg tctgcctgct 180
gcactgcttt ggtttcatca gctgttttc ccaacaaata tatggtgttg tgtatgggaa 240
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catttgaca acctgtatcc caagcagcgg tcattcaaga cacagatatg cacttatacc 780
cataccatta gcagtaatta caacatgtat tgtgctgtat atgaatggta ttctgaaatg 840
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cataactaaa ttattttaa aactaaaaag ccatctgatt tctcatttga gtattacaat 960
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<210> 12

<211> 250

<212> PRT

<213> Homo sapiens

<400> 12

Met Val Ala Gly Ser Asp Ala Gly Arg Ala Leu Gly Val Leu Ser Val

1 5 10 15

Val Cys Leu Leu His Cys Phe Gly Phe Ile Ser Cys Phe Ser Gln Gln

20 25 30

Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His Val Pro Ser Asn

35 40 45
 Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys Asp Lys Val Ala
 50 55 60
 Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser Phe Lys Asn Arg
 65 70 75 80
 Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile Tyr Asn Leu Thr
 85 90 95
 Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro Asn Ile Thr Asp
 100 105 110
 Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Leu Pro Ser Pro Thr
 115 120 125
 Leu Thr Cys Ala Leu Thr Asn Gly Ser Ile Glu Val Gln Cys Met Ile
 130 135 140
 Pro Glu His Tyr Asn Ser His Arg Gly Leu Ile Met Tyr Ser Trp Asp
 145 150 155 160
 Cys Pro Met Glu Gln Cys Lys Arg Asn Ser Thr Ser Ile Tyr Phe Lys
 165 170 175
 Met Glu Asn Asp Leu Pro Gln Lys Ile Gln Cys Thr Leu Ser Asn Pro
 180 185 190
 Leu Phe Asn Thr Thr Ser Ser Ile Ile Leu Thr Thr Cys Ile Pro Ser
 195 200 205
 Ser Gly His Ser Arg His Arg Tyr Ala Leu Ile Pro Ile Pro Leu Ala
 210 215 220
 Val Ile Thr Thr Cys Ile Val Leu Tyr Met Asn Gly Ile Leu Lys Cys
 225 230 235 240
 Asp Arg Lys Pro Asp Arg Thr Asn Ser Asn
 245 250

<210> 13

<211> 6492

<212> DNA

<213> Homo sapiens

<400> 13

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 attgatggga tcgttgccct atgcatttgt ttgggttta caaaaaggaa acttgacaga 180

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 cctgcatctc atgccaaggg ggaaacacca gaatcaagtg ttccgcgtga ttgaagacac 360

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