

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

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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

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<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

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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
115

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<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

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caggtgcaat tgggtgcagtc tggcgctgaa gttaagaagc ctgggagttc agtgaaggtc      60
tcctgcaagg cttccggata cgccttcagc tattcttggga tcaattgggt gcggcaggcg      120
cctggacaag ggctcgagtg gatgggacgg atctttcccg gcgatgggga tactgactac      180
aatgggaaat tcaagggcag agtcacaatt accgccgaca aatccactag cacagcctat      240
atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc aagaaatgtc      300
tttgatgggtt 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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gatatcgtga tgacccagac tccactctcc ctgcccgtca cccctggaga gcccgccagc      60
attagctgca ggtctagcaa gagcctcttg cacagcaatg gcatcactta tttgtattgg      120
tacctgcaaa agccagggca gtctccacag ctcttgattt atcaaatgtc caaccttgtc      180
tctggcgtcc ctgaccgggt ctccggatcc gggtcaggca ctgatttcac actgaaaatc      240
agcaggggtgg aggctgagga tgttggagtt tattactgcg ctcagaatct agaacttcct      300
tacaccttcg gcggagggac caaggtggag atcaaacgta cggtg                        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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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 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
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

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	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
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ala Gln Asn				
	85		90	
Leu Glu Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys				
	100		105	
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu				
	115		120	
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe				
	130		135	
Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln				
145		150		155
Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser				
	165		170	
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu				
	180		185	
Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser				
	195		200	
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 tattcttggga tcaattgggt gcggcaggcg	120
cctggacaag ggctcgagtg gatgggacgg atctttcccg gcgatgggga tactgactac	180
aatgggaaat tcaagggcag agtcacaatt accgccgaca aatccactag cacagcctat	240
atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc aagaaatgtc	300
tttgatgggtt actggcttgt ttactggggc cagggaaccc tggtcaccgt ctctca	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

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gatatcgtga tgacccagac tccactctcc ctgcccgtca cccctggaga gcccgccagc      60
attagctgca ggtctagcaa gagcctcttg cacagcaatg gcatcactta tttgtattgg      120
tacctgcaaa agccagggca gtctccacag ctcttgattt atcaaatgtc caaccttgct      180
tctggcgtcc ctgaccggtt ctccggatcc gggtcaggca ctgatttcac actgaaaatc      240
agcaggggtgg aggctgagga tgttggagtt tattactgcg ctcagaatct agaacttcct      300
tacaccttcg gcggagggac caaggtggag atcaaacgta cggtg                        345

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<210> 9

<211> 451

<212> PRT

<213> Artificial Sequence

<220>

<223> the heavy chain of rituximab

<400> 9

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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

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[illegible]

$\langle 210 \rangle$ 10

<211> 213

<212> PRT

<213> Artificial Sequence

$\langle 220 \rangle$

<223> the light chain of rituximab

 $\langle 400 \rangle$ 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
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
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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ggtgcttgaa cttagggctg cttgtggctg ggcaactcgcg cagaggccgg cccgacgagc	120
catggttgct gggagcgacg cggggcgggc cctggggggtc ctcagcgtgg tctgcctgct	180
gcactgcttt ggtttcatca gctgtttttc ccaacaaata tatggtgttg tgtatgggaa	240
tgtaactttc catgtaccaa gcaatgtgcc tttaaaagag gtcctatgga aaaaacaaaa	300
ggataaagtt gcagaactgg aaaattctga attcagagct ttctcatctt ttaaaaatag	360
ggtttattta gacactgtgt caggtagcct cactatctac aacttaacat catcagatga	420
agatgagtat gaaatggaat cgccaaatat tactgatacc atgaagttct ttctttatgt	480
gcttgagtct cttccatctc ccacactaac ttgtgcattg actaatggaa gcattgaagt	540
ccaatgcatg ataccagagc attacaacag ccatcgagga cttataatgt actcatggga	600

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ttgtcctatg gagcaatgta aacgtaactc aaccagtata tattttaaga tggaaaatga      660
tcttccacaa aaaatacagt gtactcttag caatccatta tttaatacaa catcatcaat      720
cattttgaca acctgtatcc caagcagcgg tcattcaaga cacagatatg cacttatacc      780
cataccatta gcagtaatta caacatgtat tgtgctgtat atgaatggta ttctgaaatg      840
tgacagaaaa ccagacagaa ccaactccaa ttgattggta acagaagatg aagacaacag      900
cataactaaa ttattttaaa aactaaaaag ccatctgatt tctcatttga gtattacaat      960
ttttgaacaa ctgttggaag tgtaacttga agcagctgct ttaagaagaa atacccacta     1020
acaaagaaca agcattagtt ttggctgtca tcaacttatt atatgactag gtgcttgctt     1080
ttttgtcag taaattgttt ttactgatga tgtagatact tttgtaaata aatgtaaata     1140
tgtacacaag tga                                                         1153

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<210> 12
<211> 250
<212> PRT
<213> Homo sapiens

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<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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ccccgcgact cctgattcat tgggaagttt caaatcagct ataactggag agtgctgaag	120
attgatggga tcgttgcctt atgcatttgt tttggtttta caaaaaggaa acttgacaga	180
ggatcatgct gtacttaaaa aataacaacat cacagaggaa gtagactgat attaacaata	240
cttactaata ataacgtgcc tcatgaaata aagatccgaa aggaattgga ataaaaattt	300
cctgcatctc atgccaaggg ggaaacacca gaatcaagtg ttccgcgtga ttgaagacac	360
cccctcgtcc aagaatgcaa agcacatcca ataaaatagc tggattataa ctctcttct	420
ttctctgggg gccgtggggt gggagctggg gcgagagggt ccgttggccc ccgttgcttt	480
tcctctggga aggatggcgc acgctgggag aacagggtac gataaccggg agatagtgat	540
gaagtacatc cattataagc tgtcgcagag gggctacgag tgggatgcgg gagatgtggg	600
cgccgcgccc ccgggggccc ccccccgcacc gggcatcttc tcctcccagc ccgggcacac	660
gccccatcca gccgcatccc gggacccggt cgccaggacc tcgccgctgc agaccccggc	720
tgcccccggc gccgccgcgg ggcctgcgct cagcccgggt ccacctgtgg tccacctgac	780
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gctcttcagg gacgggggtga actgggggag gattgtggcc ttctttgagt tcggtggggt	960
catgtgtgtg gagagcgtca accgggagat gtcgcccctg gtggacaaca tcgccctgtg	1020

gatgactgag tacctgaacc ggcacctgca cacctggatc caggataacg gaggctggga	1080
tgccctttgtg gaactgtacg gccccagcat gcggcctctg tttgatttct cctggctgtc	1140
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agtagaaaata atatgcattg tcagtgatgt accatgaaac aaagctgcag gctgtttaag	1320
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aacagtcttc aggcaaaacg tcgaatcagc tatttactgc caaagggaaa tatcatttat	1440
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taccactga gatttcacg ccgaaggaca gcgatgggaa aaatgccctt aaatcatagg	1920
aaagtatttt ttttaagctac caattgtgcc gagaaaagca ttttagcaat ttatacaata	1980
tcattccagta ccttaagccc tgattgtgta tattcatata ttttggatac gcacccccca	2040
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taaagaagta acaaaaagaag tgacatcttc agcaaataaa ctaggaaatt tttttttctt	2880
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ttatctcttg attcttcaaa agcattctga gaagggtgaga taagccctga gtctcagcta	3180
cctaagaaaa acctggatgt cactggccac tgaggagcct tgtttcaacc aagtcattgtg	3240
catttccacg tcaacagaat tgtttattgt gacagttata tctgttgtcc ctttgacctt	3300
gtttcttgaa ggtttcctcg tccctgggca attccgcatt taattcatgg tattcaggat	3360
tacatgcatg tttggttaaa cccatgagat tcattcagtt aaaaatccag atggcaaatg	3420
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tcaacacaga cccacccaga gccctcctgc cctccttccg cgggggcctt ctcattggctg	3540
tccttcaggg tcttcctgaa atgcagtgggt gcttacgctc caccaagaaa gcaggaaacc	3600
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