

SEQUENCE LISTING

<110> JCR Pharmaceuticals Co., Ltd.

<120> Stable liquid pharmaceutical composition and lyophilized pharmaceutical composition

<130> 1230JP

<150> JP 2021-049485

<151> 2021-03-24

<160> 42

<170> PatentIn version 3.5

<210> 1

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of an exemplified linker 1

<400> 1

Gly Gly Gly Gly Ser
1 5

<210> 2

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of an exemplified linker 2

<400> 2

Gly Gly Gly Gly Gly Ser
1 5

<210> 3

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of an exemplified linker 3

<400> 3

Ser Gly Gly Gly Gly

1 5

<210> 4

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of an exemplified linker 4

<400> 4

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

1 5 10 15

<210> 5

<211> 760

<212> PRT

<213> Homo sapiens

<400> 5

Met Met Asp Gln Ala Arg Ser Ala Phe Ser Asn Leu Phe Gly Gly Glu

1 5 10 15

Pro Leu Ser Tyr Thr Arg Phe Ser Leu Ala Arg Gln Val Asp Gly Asp

20 25 30

Asn Ser His Val Glu Met Lys Leu Ala Val Asp Glu Glu Glu Asn Ala

35 40 45

Asp Asn Asn Thr Lys Ala Asn Val Thr Lys Pro Lys Arg Cys Ser Gly

50 55 60

Ser Ile Cys Tyr Gly Thr Ile Ala Val Ile Val Phe Phe Leu Ile Gly

65 70 75 80

Phe Met Ile Gly Tyr Leu Gly Tyr Cys Lys Gly Val Glu Pro Lys Thr
85 90 95

Glu Cys Glu Arg Leu Ala Gly Thr Glu Ser Pro Val Arg Glu Glu Pro
100 105 110

Gly Glu Asp Phe Pro Ala Ala Arg Arg Leu Tyr Trp Asp Asp Leu Lys
115 120 125

Arg Lys Leu Ser Glu Lys Leu Asp Ser Thr Asp Phe Thr Gly Thr Ile
130 135 140

Lys Leu Leu Asn Glu Asn Ser Tyr Val Pro Arg Glu Ala Gly Ser Gln
145 150 155 160

Lys Asp Glu Asn Leu Ala Leu Tyr Val Glu Asn Gln Phe Arg Glu Phe
165 170 175

Lys Leu Ser Lys Val Trp Arg Asp Gln His Phe Val Lys Ile Gln Val
180 185 190

Lys Asp Ser Ala Gln Asn Ser Val Ile Ile Val Asp Lys Asn Gly Arg
195 200 205

Leu Val Tyr Leu Val Glu Asn Pro Gly Gly Tyr Val Ala Tyr Ser Lys
210 215 220

Ala Ala Thr Val Thr Gly Lys Leu Val His Ala Asn Phe Gly Thr Lys
225 230 235 240

Lys Asp Phe Glu Asp Leu Tyr Thr Pro Val Asn Gly Ser Ile Val Ile
245 250 255

Val Arg Ala Gly Lys Ile Thr Phe Ala Glu Lys Val Ala Asn Ala Glu
260 265 270

Ser Leu Asn Ala Ile Gly Val Leu Ile Tyr Met Asp Gln Thr Lys Phe
275 280 285

Pro Ile Val Asn Ala Glu Leu Ser Phe Phe Gly His Ala His Leu Gly
290 295 300

Thr Gly Asp Pro Tyr Thr Pro Gly Phe Pro Ser Phe Asn His Thr Gln
305 310 315 320

Phe Pro Pro Ser Arg Ser Ser Gly Leu Pro Asn Ile Pro Val Gln Thr
325 330 335

Ile Ser Arg Ala Ala Ala Glu Lys Leu Phe Gly Asn Met Glu Gly Asp
340 345 350

Cys Pro Ser Asp Trp Lys Thr Asp Ser Thr Cys Arg Met Val Thr Ser
355 360 365

Glu Ser Lys Asn Val Lys Leu Thr Val Ser Asn Val Leu Lys Glu Ile
370 375 380

Lys Ile Leu Asn Ile Phe Gly Val Ile Lys Gly Phe Val Glu Pro Asp
385 390 395 400

His Tyr Val Val Val Gly Ala Gln Arg Asp Ala Trp Gly Pro Gly Ala
405 410 415

Ala Lys Ser Gly Val Gly Thr Ala Leu Leu Lys Leu Ala Gln Met
420 425 430

Phe Ser Asp Met Val Leu Lys Asp Gly Phe Gln Pro Ser Arg Ser Ile
435 440 445

Ile Phe Ala Ser Trp Ser Ala Gly Asp Phe Gly Ser Val Gly Ala Thr
450 455 460

Glu Trp Leu Glu Gly Tyr Leu Ser Ser Leu His Leu Lys Ala Phe Thr

465		470		475		480
Tyr Ile Asn Leu Asp Lys Ala Val Leu Gly Thr Ser Asn Phe Lys Val						
		485		490		495
Ser Ala Ser Pro Leu Leu Tyr Thr Leu Ile Glu Lys Thr Met Gln Asn						
		500		505		510
Val Lys His Pro Val Thr Gly Gln Phe Leu Tyr Gln Asp Ser Asn Trp						
		515		520		525
Ala Ser Lys Val Glu Lys Leu Thr Leu Asp Asn Ala Ala Phe Pro Phe						
		530		535		540
Leu Ala Tyr Ser Gly Ile Pro Ala Val Ser Phe Cys Phe Cys Glu Asp						
545		550		555		560
Thr Asp Tyr Pro Tyr Leu Gly Thr Thr Met Asp Thr Tyr Lys Glu Leu						
		565		570		575
Ile Glu Arg Ile Pro Glu Leu Asn Lys Val Ala Arg Ala Ala Ala Glu						
		580		585		590
Val Ala Gly Gln Phe Val Ile Lys Leu Thr His Asp Val Glu Leu Asn						
		595		600		605
Leu Asp Tyr Glu Arg Tyr Asn Ser Gln Leu Leu Ser Phe Val Arg Asp						
		610		615		620
Leu Asn Gln Tyr Arg Ala Asp Ile Lys Glu Met Gly Leu Ser Leu Gln						
625		630		635		640
Trp Leu Tyr Ser Ala Arg Gly Asp Phe Phe Arg Ala Thr Ser Arg Leu						
		645		650		655
Thr Thr Asp Phe Gly Asn Ala Glu Lys Thr Asp Arg Phe Val Met Lys						
		660		665		670

Lys Leu Asn Asp Arg Val Met Arg Val Glu Tyr His Phe Leu Ser Pro
675 680 685

Tyr Val Ser Pro Lys Glu Ser Pro Phe Arg His Val Phe Trp Gly Ser
690 695 700

Gly Ser His Thr Leu Pro Ala Leu Leu Glu Asn Leu Lys Leu Arg Lys
705 710 715 720

Gln Asn Asn Gly Ala Phe Asn Glu Thr Leu Phe Arg Asn Gln Leu Ala
725 730 735

Leu Ala Thr Trp Thr Ile Gln Gly Ala Ala Asn Ala Leu Ser Gly Asp
740 745 750

Val Trp Asp Ile Asp Asn Glu Phe
755 760

<210> 6
<211> 628
<212> PRT
<213> Homo sapiens

<400> 6

Ala Glu Ala Pro His Leu Val His Val Asp Ala Ala Arg Ala Leu Trp
1 5 10 15

Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu Pro
20 25 30

His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu Asn
35 40 45

Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg
50 55 60

Thr His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg
65 70 75 80

Gly Leu Ser Tyr Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu Leu
85 90 95

Arg Glu Asn Gln Leu Leu Pro Gly Phe Glu Leu Met Gly Ser Ala Ser
100 105 110

Gly His Phe Thr Asp Phe Glu Asp Lys Gln Gln Val Phe Glu Trp Lys
115 120 125

Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg Tyr Gly Leu
130 135 140

Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His
145 150 155 160

His Asp Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr
165 170 175

Tyr Asp Ala Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg
180 185 190

Leu Gly Gly Pro Gly Asp Ser Phe His Thr Pro Pro Arg Ser Pro Leu
195 200 205

Ser Trp Gly Leu Leu Arg His Cys His Asp Gly Thr Asn Phe Phe Thr
210 215 220

Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys Gly
225 230 235 240

Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala Gln
245 250 255

Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn

260

265

270

Asp Glu Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp Arg
 275 280 285

Ala Asp Val Thr Tyr Ala Ala Met Val Val Lys Val Ile Ala Gln His
 290 295 300

Gln Asn Leu Leu Leu Ala Asn Thr Thr Ser Ala Phe Pro Tyr Ala Leu
 305 310 315 320

Leu Ser Asn Asp Asn Ala Phe Leu Ser Tyr His Pro His Pro Phe Ala
 325 330 335

Gln Arg Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg Pro Pro
 340 345 350

His Val Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu Leu
 355 360 365

Ala Leu Leu Asp Glu Glu Gln Leu Trp Ala Glu Val Ser Gln Ala Gly
 370 375 380

Thr Val Leu Asp Ser Asn His Thr Val Gly Val Leu Ala Ser Ala His
 385 390 395 400

Arg Pro Gln Gly Pro Ala Asp Ala Trp Arg Ala Ala Val Leu Ile Tyr
 405 410 415

Ala Ser Asp Asp Thr Arg Ala His Pro Asn Arg Ser Val Ala Val Thr
 420 425 430

Leu Arg Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val Tyr Val Thr
 435 440 445

Arg Tyr Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp Arg Arg
 450 455 460

Leu Gly Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg
465 470 475 480

Ala Ala Glu Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly
485 490 495

Gly Arg Leu Thr Leu Arg Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu
500 505 510

Val His Val Cys Ala Arg Pro Glu Lys Pro Pro Gly Gln Val Thr Arg
515 520 525

Leu Arg Ala Leu Pro Leu Thr Gln Gly Gln Leu Val Leu Val Trp Ser
530 535 540

Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln Phe
545 550 555 560

Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser Thr
565 570 575

Phe Asn Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser
580 585 590

Tyr Arg Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser
595 600 605

Asp Pro Val Pro Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro Ser
610 615 620

Pro Gly Asn Pro
625

<210> 7
<211> 626
<212> PRT

<213> Homo sapiens

<400> 7

Ala Pro His Leu Val His Val Asp Ala Ala Arg Ala Leu Trp Pro Leu
1 5 10 15

Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu Pro His Ser
20 25 30

Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu Asn Leu Ala
35 40 45

Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg Thr His
50 55 60

Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu
65 70 75 80

Ser Tyr Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu
85 90 95

Asn Gln Leu Leu Pro Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His
100 105 110

Phe Thr Asp Phe Glu Asp Lys Gln Gln Val Phe Glu Trp Lys Asp Leu
115 120 125

Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg Tyr Gly Leu Ala His
130 135 140

Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His His Asp
145 150 155 160

Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp
165 170 175

Ala Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly

180

185

190

Gly Pro Gly Asp Ser Phe His Thr Pro Pro Arg Ser Pro Leu Ser Trp
 195 200 205

Gly Leu Leu Arg His Cys His Asp Gly Thr Asn Phe Phe Thr Gly Glu
 210 215 220

Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys Gly Ala Arg
 225 230 235 240

Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala Gln Gln Ile
 245 250 255

Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu
 260 265 270

Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp Arg Ala Asp
 275 280 285

Val Thr Tyr Ala Ala Met Val Val Lys Val Ile Ala Gln His Gln Asn
 290 295 300

Leu Leu Leu Ala Asn Thr Thr Ser Ala Phe Pro Tyr Ala Leu Leu Ser
 305 310 315 320

Asn Asp Asn Ala Phe Leu Ser Tyr His Pro His Pro Phe Ala Gln Arg
 325 330 335

Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg Pro Pro His Val
 340 345 350

Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu Leu Ala Leu
 355 360 365

Leu Asp Glu Glu Gln Leu Trp Ala Glu Val Ser Gln Ala Gly Thr Val
 370 375 380

Leu Asp Ser Asn His Thr Val Gly Val Leu Ala Ser Ala His Arg Pro
385 390 395 400

Gln Gly Pro Ala Asp Ala Trp Arg Ala Ala Val Leu Ile Tyr Ala Ser
405 410 415

Asp Asp Thr Arg Ala His Pro Asn Arg Ser Val Ala Val Thr Leu Arg
420 425 430

Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val Tyr Val Thr Arg Tyr
435 440 445

Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp Arg Arg Leu Gly
450 455 460

Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala
465 470 475 480

Glu Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg
485 490 495

Leu Thr Leu Arg Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His
500 505 510

Val Cys Ala Arg Pro Glu Lys Pro Pro Gly Gln Val Thr Arg Leu Arg
515 520 525

Ala Leu Pro Leu Thr Gln Gly Gln Leu Val Leu Val Trp Ser Asp Glu
530 535 540

His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln Phe Ser Gln
545 550 555 560

Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asn
565 570 575

Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg
580 585 590

Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro
595 600 605

Val Pro Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro Ser Pro Gly
610 615 620

Asn Pro
625

<210> 8
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 1 of CDR 1 in the light chain of anti-hTfR
antibody

<400> 8

Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr
1 5 10

<210> 9
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 2 of CDR 1 in the light chain of anti-hTfR
antibody

<400> 9

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
1 5 10 15

<210> 10
<211> 6

<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 1 of CDR 2 in the light chain of anti-hTfR antibody

<400> 10

Lys Val Ser Asn Arg Phe
1 5

<210> 11
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 2 of CDR 2 in the light chain of anti-hTfR antibody

<400> 11

Lys Val Ser Asn Arg Phe Ser
1 5

<210> 12
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of CDR 3 in the light chain of anti-hTfR antibody

<400> 12

Ser Gln Ser Thr His Val Pro Trp Thr
1 5

<210> 13
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Amino acid sequence 1 of CDR1 in the heavy chain of anti-hTfR antibody

<400> 13

Gly Tyr Ser Phe Met Asn Tyr Trp
1 5

<210> 14

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence 2 of CDR1 in the heavy chain of anti-hTfR antibody

<400> 14

Gly Tyr Ser Phe Met Asn Tyr Trp Leu Gly
1 5 10

<210> 15

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence 1 of CDR 2 in the heavy chain of anti-hTfR antibody

<400> 15

Ile Tyr Pro Gly Gly Asp Tyr Pro
1 5

<210> 16

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence 2 of CDR 2 in the heavy chain of anti-hTfR antibody

<400> 16

Asp Ile Tyr Pro Gly Gly Asp Tyr Pro Thr Tyr Ser Glu Lys Phe Lys
1 5 10 15

Val

<210> 17
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 1 of CDR 3 in the heavy chain of anti-hTfR antibody

<400> 17

Ser Gly Asn Tyr Asp Glu Val Ala Tyr
1 5

<210> 18
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence 2 of CDR 3 in the heavy chain of anti-hTfR antibody

<400> 18

Ala Arg Ser Gly Asn Tyr Asp Glu Val Ala Tyr
1 5 10

<210> 19
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of framework region 3 in the heavy chain of anti-hTfR antibody

<400> 19

Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr Leu Gln
 1 5 10 15

Leu Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
 20 25 30

<210> 20
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Amino acid sequence of the variable region of the light chain
 of anti-hTfR antibody

<400> 20

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
 1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
 20 25 30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe 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 Ser Gln Ser
 85 90 95

Thr His Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 21

<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of the variable region of the heavy chain of anti-hTfR antibody

<400> 21

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Met Asn Tyr
20 25 30

Trp Leu Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Asp Ile Tyr Pro Gly Gly Asp Tyr Pro Thr Tyr Ser Glu Lys Phe
50 55 60

Lys Val Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Leu Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Asn Tyr Asp Glu Val Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 22
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of the light chain of anti-hTfR antibody

<400> 22

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe 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 Ser Gln Ser
85 90 95

Thr His Val Pro Trp Thr Phe Gly Gln 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> 23
<211> 226
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acid sequence of Fab-heavy chain of anti-hTfR antibody

<400> 23

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Met Asn Tyr
20 25 30

Trp Leu Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Asp Ile Tyr Pro Gly Gly Asp Tyr Pro Thr Tyr Ser Glu Lys Phe
50 55 60

Lys Val Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Leu Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Asn Tyr Asp Glu Val Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro

115

120

125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
 130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
 145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
 165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
 180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
 195 200 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
 210 215 220

His Thr
 225

<210> 24
 <211> 20
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer Hyg-Sfi5', synthetic sequence

<400> 24
 gaggccgcct cggcctctga 20

<210> 25
 <211> 29
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Primer Hyg-BstX3', synthetic sequence

<400> 25

aaccatcgtg atgggtgcta ttcctttgc

29

<210> 26

<211> 740

<212> DNA

<213> Artificial Sequence

<220>

<223> Nucleotide sequence encoding the amino acid sequence of the light chain of anti-hTfR antibody, synthetic sequence

<400> 26

acgcgtgccg ccaccatggg ctggagctgg attctgctgt tcctcctgag cgtgacagca 60

ggagtgcaca gcgacatcgt gatgaccag actcccctga gcctgagcgt gacacctggc 120

cagcctgcc a gcatcagctg cagaagctct cagagcctgg tgcacagcaa cggcaacacc 180

tacctgcact ggtatctgca gaagcccggc cagagccctc agctgctgat ctacaagggtg 240

tccaacagat tcagcggcgt gcccagacaga ttctccggca gcggctctgg caccgacttc 300

accctgaaga tttccagagt ggaagccgag gacgtgggcg tgtactactg cagccagagc 360

accacgtgc cctggacatt cggccagggc accaagggtg aaatcaagag aaccgtggcc 420

gctcccagcg tgttcatctt cccacctagc gacgagcagc tgaagtccgg cacagcctct 480

gtcgtgtgcc tgctgaacaa cttctacccc cgcgaggcca aggtgcagtg gaagggtggac 540

aacgccctgc agagcggcaa cagccaggaa agcgtgaccg agcaggactc caaggacagc 600

acctacagcc tgagcagcac cctgaccctg agcaaggccg actacgagaa gcacaagggtg 660

tacgcctgcg aagtgaccca ccagggcctg tctagccccg tgaccaagag cttcaacaga 720

ggcgagtgct aagcggccgc 740

<210> 27

<211> 869

<212> PRT

<213> Artificial Sequence

<220>

<223> Amino acid sequence of fusion protein of the Fab-heavy chain of anti-hTfR antibody and hIDUA

<400> 27

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Met Asn Tyr
20 25 30

Trp Leu Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Asp Ile Tyr Pro Gly Gly Asp Tyr Pro Thr Tyr Ser Glu Lys Phe
50 55 60

Lys Val Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Leu Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Asn Tyr Asp Glu Val Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195 200 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
210 215 220

His Thr Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
225 230 235 240

Ser Ala Glu Ala Pro His Leu Val His Val Asp Ala Ala Arg Ala Leu
245 250 255

Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe Cys Pro Pro Leu
260 265 270

Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln Leu
275 280 285

Asn Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val
290 295 300

Arg Thr His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly
305 310 315 320

Arg Gly Leu Ser Tyr Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu
325 330 335

Leu Arg Glu Asn Gln Leu Leu Pro Gly Phe Glu Leu Met Gly Ser Ala
340 345 350

Ser Gly His Phe Thr Asp Phe Glu Asp Lys Gln Gln Val Phe Glu Trp
355 360 365

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

370

375

380

Leu Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp
 385 390 395 400

His His Asp Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn
 405 410 415

Tyr Tyr Asp Ala Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu
 420 425 430

Arg Leu Gly Gly Pro Gly Asp Ser Phe His Thr Pro Pro Arg Ser Pro
 435 440 445

Leu Ser Trp Gly Leu Leu Arg His Cys His Asp Gly Thr Asn Phe Phe
 450 455 460

Thr Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu His Arg Lys
 465 470 475 480

Gly Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala
 485 490 495

Gln Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr
 500 505 510

Asn Asp Glu Ala Asp Pro Leu Val Gly Trp Ser Leu Pro Gln Pro Trp
 515 520 525

Arg Ala Asp Val Thr Tyr Ala Ala Met Val Val Lys Val Ile Ala Gln
 530 535 540

His Gln Asn Leu Leu Leu Ala Asn Thr Thr Ser Ala Phe Pro Tyr Ala
 545 550 555 560

Leu Leu Ser Asn Asp Asn Ala Phe Leu Ser Tyr His Pro His Pro Phe
 565 570 575

Ala Gln Arg Thr Leu Thr Ala Arg Phe Gln Val Asn Asn Thr Arg Pro
580 585 590

Pro His Val Gln Leu Leu Arg Lys Pro Val Leu Thr Ala Met Gly Leu
595 600 605

Leu Ala Leu Leu Asp Glu Glu Gln Leu Trp Ala Glu Val Ser Gln Ala
610 615 620

Gly Thr Val Leu Asp Ser Asn His Thr Val Gly Val Leu Ala Ser Ala
625 630 635 640

His Arg Pro Gln Gly Pro Ala Asp Ala Trp Arg Ala Ala Val Leu Ile
645 650 655

Tyr Ala Ser Asp Asp Thr Arg Ala His Pro Asn Arg Ser Val Ala Val
660 665 670

Thr Leu Arg Leu Arg Gly Val Pro Pro Gly Pro Gly Leu Val Tyr Val
675 680 685

Thr Arg Tyr Leu Asp Asn Gly Leu Cys Ser Pro Asp Gly Glu Trp Arg
690 695 700

Arg Leu Gly Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met
705 710 715 720

Arg Ala Ala Glu Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala
725 730 735

Gly Gly Arg Leu Thr Leu Arg Pro Ala Leu Arg Leu Pro Ser Leu Leu
740 745 750

Leu Val His Val Cys Ala Arg Pro Glu Lys Pro Pro Gly Gln Val Thr
755 760 765

Arg Leu Arg Ala Leu Pro Leu Thr Gln Gly Gln Leu Val Leu Val Trp
 770 775 780

Ser Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln
 785 790 795 800

Phe Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser
 805 810 815

Thr Phe Asn Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly
 820 825 830

Ser Tyr Arg Val Arg Ala Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe
 835 840 845

Ser Asp Pro Val Pro Tyr Leu Glu Val Pro Val Pro Arg Gly Pro Pro
 850 855 860

Ser Pro Gly Asn Pro
 865

<210> 28
 <211> 2688
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Nucleotide seuquence encoding the amino acid sequence of fusion
 protein of the Fab-heavy chain of anti-hTfR antibody and hIDUA,
 synthetic sequence

<400> 28
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 agtcggcagc gaggtgcaac tagtgcagtc tggagcagag gtgaaaaagc cgggggagtc 120
 tctgaagatt tcctgtaagg gttctggata cagctttatg aactactggc tgggatgggt 180
 gcgccagatg cccgggaaag gcctggagtg gatggggggac atctaccccg gcggagacta 240
 ccctacatac agcgagaagt tcaaggtcca ggtcaccatc tcagccgaca agtccatcag 300

caccgcctac ctgcagttga gcagcctgaa ggccctcggac accgccatgt attactgtgc	360
gagatcaggc aattacgacg aagtggccta ctggggccaa ggaaccctgg tcaccgtctc	420
ctcagctagc accaagggcc catcgggtctt ccccctggca ccctcctcca agagcacctc	480
tgggggcaca gcggccctgg gctgcctggg caaggactac ttccccgaac cgggtgacggg	540
gtcgtggaac tcaggcgccc tgaccagcgg cgtgcacacc ttcccggctg tcctacagtc	600
ctcaggactc tactccctca gcagcgtggg gaccgtgccc tccagcagct tgggcaccca	660
gacctacatc tgcaacgtga atcacaagcc cagcaacacc aagggtggaca agaaagttga	720
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gcagatccgg cagctcttcc ccaagtctgc ggacaccccc atttacaacg acgaggcgga	1620
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cggggtgccc cccggcccgg gcctgggtcta cgtcacgcgc tacctggaca acgggctctg	2160
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cttcaacctc tttgtgttca gcccagacac aggtgctgtc tctggctcct accgagttcg	2580
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<210> 29
 <211> 53
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer IRES5', synthetic sequence

<400> 29	
caactcgagc ggccgcccc cccccctctc cctccccccc ccctaacgtt act	53

<210> 30
 <211> 22
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer IRES3', synthetic sequence

 <400> 30
 caagaagctt ccagaggaac tg 22

 <210> 31
 <211> 30
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Primer mPGKP5', synthetic sequence

 <400> 31
 gcgagatctt accgggtagg ggaggcgctt 30

 <210> 32
 <211> 30
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Primer mPGKP3', synthetic sequence

 <400> 32
 gaggaattcg atgatcggtc gaaaggcccg 30

 <210> 33
 <211> 36
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> Primer GS5', synthetic sequence

 <400> 33
 aatatggcca caaccatggc gacctcagca agttcc 36

 <210> 34
 <211> 38
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer GS3', synthetic sequence

<400> 34
 ggaggatccc tcgagttagt ttttgtattg gaagggct 38

<210> 35
 <211> 28
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer puro5', synthetic sequence

<400> 35
 gcttaagatg accgagtaca agcccacg 28

<210> 36
 <211> 30
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer puro3', synthetic sequence

<400> 36
 cccatcgtga tggtcaggca ccgggcttgc 30

<210> 37
 <211> 44
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer SV40polyA5', synthetic sequence

<400> 37
 caacaagcgg ccgccctcga gttcccttta gtgagggtta atgc 44

<210> 38
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Primer SV40polyA3', synthetic sequence

<400> 38
cccctgaacc tgaaacataa aatg 24

<210> 39
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer mIRES-GS5', synthetic sequence

<400> 39
acacgatgat aagcttgcca caacc 25

<210> 40
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer mIRES-GS3', synthetic sequence

<400> 40
ctccacgata tccctgccat a 21

<210> 41
<211> 2076
<212> DNA
<213> Artificial Sequence

<220>
<223> CMVE-EF-1 alpha p-IFN beta MAR, synthetic sequence

<400> 41
aagcttaaat tatctctaag gcatgtgaac tggctgtctt ggttttcatc tgtacttcat 60
ctgctacctc tgtgacctga aacatattta taattccatt aagctgtgca tatgatagat 120
ttatcatatg tattttcctt aaaggatttt tgtaagaact aattgaattg atacctgtaa 180
agtctttatc acactaccca ataaataata aatctctttg ttcagctctc tgtttctata 240
aatatgtacc agttttattg ttttttagtgg tagtgatttt attctctttc tatatatata 300

cacacacatg tgtgcattca taaatatata caatTTTTat gaataaaaaa ttattagcaa	360
tcaatattga aaaccactga tttttgttta tgtgagcaaa cagcagatta aaagaaattc	420
ctgcaggagt caatgggaaa aaccatttgg agccaagtac actgactcaa tagggacttt	480
ccattgggtt ttgccagta cataaggtca atagggggtg agtcaacagg aaagtcccat	540
tggagccaag tacattgagt caataggac tttccaatgg gttttgcca gtacataagg	600
tcaatgggag gtaagccaat gggTTTTcc cattactgac atgtatactg agtcattagg	660
gactttccaa tgggttttgc ccagtacata aggtcaatag gggTgaatca acaggaaagt	720
cccattggag ccaagtacac tgagtcaata gggactttcc attgggtttt gcccagtaca	780
aaaggtcaat agggggtgag tcaatgggtt tttcccatta ttggcacata cataaggtca	840
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agcacatggc ccacagtccc tgagaagttg gggggagggg tgggcaattg aactggtgcc	960
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tccccagggt gggggagaac catatataag tgcagtagtc tctgtgaaca ttcaagggtc	1080
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tctaaaatgt atatagaagc ccaaaagaca ataacaaaaa tattcttgta gaacaaaatg	1380
ggaaagaatg ttccactaaa tatcaagatt tagagcaaag catgagatgt gtggggatag	1440
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tcaaagtcct aaccacaaag aaaagattgt taattagatt gcatgaatat taagacttat	1800

ttttaaaatt aaaaaacat taagaaaagt caggccatag aatgacagaa aatatttgca	1860
acaccccagt aaagagaatt gtaatatgca gattataaaa agaagtctta caaatcagta	1920
aaaaataaaa ctagacaaaa atttgaacag atgaaagaga aactctaaat aatcattaca	1980
catgagaaac tcaatctcag aaatcagaga actatcattg catatacact aaattagaga	2040
aatattaaaa ggctaagtaa catctgtggc gaattc	2076

<210> 42
 <211> 2130
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> IRES-HygroR-mPGKpA, synthetic sequence

<400> 42	
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gcgaagaatc tcgtgctttc agcttcgatg taggagggcg tggatatgtc ctgcgggtaa	780
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cgctcccgat tccggaagtg cttgacattg gggaattcag cgagagcctg acctattgca	900
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