

6162223\_1  
SEQUENCE LISTING

<110> National Cancer Center Japan  
RIN Institute Inc.

<120> Antibody-Drug Conjugate with a plasmin cleavable linker

<130> PR15-9004SG

<150> JP2017-091639  
<151> 2017-05-02

<160> 28

<170> PatentIn version 3.5

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Asn Tyr Gly Met Asn  
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<400> 2  
Trp Ile Asn Thr Lys Ile Gly Glu Pro Thr Tyr Ala Glu Glu Phe Lys  
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Gly

<210> 3  
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Leu Leu Asp Tyr  
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&lt;223&gt; 99-5 VH

&lt;400&gt; 4

Met Asp Trp Leu Trp Asn Leu Leu Phe Leu Met Ala Ala Ala Gln Ser  
1 5 10 15Ile Gln Ala Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys  
20 25 30Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe  
35 40 45Thr Asn Tyr Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu  
50 55 60Lys Trp Met Gly Trp Ile Asn Thr Lys Ile Gly Glu Pro Thr Tyr Ala  
65 70 75 80Glu Glu Phe Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser  
85 90 95Thr Ala Tyr Leu Gln Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr  
100 105 110Tyr Phe Cys Ala Arg Leu Leu Asp Tyr Trp Gly Gln Gly Thr Thr Leu  
115 120 125Thr Val Ser Ser Ala Lys Thr Thr Pro Pro Ser Val  
130 135 140

&lt;210&gt; 5

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; 99-5 LCDR1

&lt;400&gt; 5

Arg Ala Ser Glu Ser Val Asp Ser Tyr Gly Asn Ser Phe Met His  
1 5 10 15

&lt;210&gt; 6

&lt;211&gt; 7

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

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&lt;223&gt; 99-5 LCDR2

&lt;400&gt; 6

Arg Ala Ser Asn Leu Glu Ser  
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<210> 7  
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<220>  
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<400> 7

Gln Gln Ser Asn Glu Asp Pro Arg Thr  
1 5

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<220>  
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<400> 8

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro  
1 5 10 15

Gly Ser Thr Gly Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala  
20 25 30

Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser  
35 40 45

Val Asp Ser Tyr Gly Asn Ser Phe Met His Trp Tyr Gln Gln Lys Pro  
50 55 60

Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser  
65 70 75 80

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr  
85 90 95

Leu Thr Ile Asn Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys  
100 105 110

Gln Gln Ser Asn Glu Asp Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu  
115 120 125

Glu Ile Lys Arg Ala Asp Ala Ala Pro Thr Val Ser  
130 135 140

<210> 9  
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&lt;400&gt; 9

Ser Tyr Trp Met His  
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&lt;210&gt; 10

&lt;211&gt; 17

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; 1101 HCDR2

&lt;400&gt; 10

Ala Ile Tyr Pro Gly Asn Ser Asp Thr Arg Asn Asn Gln Lys Phe Lys  
1 5 10 15

Gly

&lt;210&gt; 11

&lt;211&gt; 11

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; 1101 HCDR3

&lt;400&gt; 11

Lys Ala His Tyr Gly Asn Tyr Gly Phe Ala Tyr  
1 5 10

&lt;210&gt; 12

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; 1101 VH

&lt;400&gt; 12

Met Glu Cys Asn Trp Ile Leu Pro Phe Ile Leu Ser Val Ile Ser Gly  
1 5 10 15

Val Tyr Ser Glu Val Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg  
20 25 30

Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Phe Ser Phe  
35 40 45

Thr Ser Tyr Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu  
50 55 60

Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Ser Asp Thr Arg Asn Asn  
65 70 75 80

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Gln Lys Phe Lys Gly Lys Ala Lys Leu Thr Ala Val Thr Ser Ala Asn  
                   85                  90                  95

Thr Ala Tyr Met Glu Leu Ser Ser Leu Thr Asn Glu Asp Ser Ala Val  
                   100                  105                  110

Tyr Tyr Cys Thr Arg Lys Ala His Tyr Gly Asn Tyr Gly Phe Ala Tyr  
           115                  120                  125

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala Ala  
       130                  135                  140

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<220>  
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<400> 13

Lys Ala Ser Asp His Ile Asn Asn Trp Leu Ala  
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<220>  
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<400> 14

Gly Ala Thr Ser Leu Glu Thr  
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<400> 15

Gln Gln Tyr Trp Ser Thr Pro Leu Thr  
 1                  5

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<400> 16

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Met Ser Gly His Ser Arg Asn Met Lys Phe Pro Ser Gln Leu Leu Leu  
 1 5 10 15

Phe Leu Leu Phe Arg Ile Thr Gly Ile Ile Cys Asp Ile Gln Met Thr  
 20 25 30

Gln Ser Ser Ser Tyr Leu Ser Val Ser Leu Gly Gly Arg Val Thr Ile  
 35 40 45

Thr Cys Lys Ala Ser Asp His Ile Asn Asn Trp Leu Ala Trp Tyr Gln  
 50 55 60

Gln Lys Pro Gly Asn Ala Pro Arg Leu Leu Ile Ser Gly Ala Thr Ser  
 65 70 75 80

Leu Glu Thr Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Lys  
 85 90 95

Asp Tyr Thr Leu Ser Ile Thr Ser Leu Gln Thr Glu Asp Val Ala Thr  
 100 105 110

Tyr Tyr Cys Gln Gln Tyr Trp Ser Thr Pro Leu Thr Phe Gly Ala Gly  
 115 120 125

Thr Lys Leu Glu Leu Lys Arg Ala Asp Ala Ala Pro  
 130 135 140

<210> 17  
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<220>  
 <223> 0211 HCDR

<400> 17

Ser Tyr Ala Met Ser  
 1 5

<210> 18  
 <211> 16  
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<220>  
 <223> 0211 HCDR2

<400> 18

Ala Ile Ser Ser Gly Gly Thr Thr Tyr Tyr Pro Asp Ser Val Lys Gly  
 1 5 10 15

<210> 19  
 <211> 8  
 <212> PRT  
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<220>  
 <223> 0211 HCDR3

<400> 19

Gly Gly Thr Ile Gly Ala Tyr Trp  
 1 5

<210> 20  
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<220>  
 <223> 0211 VH

<400> 20

Met Asn Phe Gly Phe Ser Leu Ile Phe Leu Val Leu Val Leu Lys Gly  
 1 5 10 15

Val Gln Cys Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Lys  
 20 25 30

Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe  
 35 40 45

Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu  
 50 55 60

Glu Trp Val Ala Ala Ile Ser Ser Gly Gly Thr Thr Tyr Tyr Pro Asp  
 65 70 75 80

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Arg Asn Ile  
 85 90 95

Leu Tyr Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr  
 100 105 110

Tyr Cys Val Arg Gly Gly Thr Ile Gly Ala Tyr Trp Gly Gln Gly Thr  
 115 120 125

Leu Val Thr Val Ser Ala  
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<400> 21

Lys Ser Ser Gln Ser Val Leu Tyr Ser Ser Asn Gln Lys Asn Tyr Leu  
 1 5 10 15

Ala

<210> 22  
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<400> 22

Trp Ala Ser Thr Arg Glu Ser  
 1 5

<210> 23  
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<400> 23

His Gln Tyr Leu Ser Ser Trp Thr  
 1 5

<210> 24  
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<220>  
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<400> 24

Met Glu Ser Gln Thr Gln Val Phe Leu Ser Leu Leu Leu Trp Val Ser  
 1 5 10 15

Gly Thr Cys Gly Asn Ile Met Met Thr Gln Ser Pro Ser Ser Leu Ala  
 20 25 30

Val Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser  
 35 40 45

Val Leu Tyr Ser Ser Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln  
 50 55 60

Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg  
 65 70 75 80

Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp  
 85 90 95

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Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr  
 100 105 110

Tyr Cys His Gln Tyr Leu Ser Ser Trp Thr Phe Gly Gly Gly Thr Lys  
 115 120 125

Leu Glu Ile Lys  
 130

<210> 25  
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 <212> PRT  
 <213> Homo sapiens

<400> 25

Met Lys Arg Met Val Ser Trp Ser Phe His Lys Leu Lys Thr Met Lys  
 1 5 10 15

His Leu Leu Leu Leu Leu Cys Val Phe Leu Val Lys Ser Gln Gly  
 20 25 30

Val Asn Asp Asn Glu Glu Gly Phe Phe Ser Ala Arg Gly His Arg Pro  
 35 40 45

Leu Asp Lys Lys Arg Glu Glu Ala Pro Ser Leu Arg Pro Ala Pro Pro  
 50 55 60

Pro Ile Ser Gly Gly Gly Tyr Arg Ala Arg Pro Ala Lys Ala Ala Ala  
 65 70 75 80

Thr Gln Lys Lys Val Glu Arg Lys Ala Pro Asp Ala Gly Gly Cys Leu  
 85 90 95

His Ala Asp Pro Asp Leu Gly Val Leu Cys Pro Thr Gly Cys Gln Leu  
 100 105 110

Gln Glu Ala Leu Leu Gln Gln Glu Arg Pro Ile Arg Asn Ser Val Asp  
 115 120 125

Glu Leu Asn Asn Asn Val Glu Ala Val Ser Gln Thr Ser Ser Ser Ser  
 130 135 140

Phe Gln Tyr Met Tyr Leu Leu Lys Asp Leu Trp Gln Lys Arg Gln Lys  
 145 150 155 160

Gln Val Lys Asp Asn Glu Asn Val Val Asn Glu Tyr Ser Ser Glu Leu  
 165 170 175

Glu Lys His Gln Leu Tyr Ile Asp Glu Thr Val Asn Ser Asn Ile Pro  
 180 185 190

Thr Asn Leu Arg Val Leu Arg Ser Ile Leu Glu Asn Leu Arg Ser Lys  
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195

200

205

Ile Gln Lys Leu Glu Ser Asp Val Ser Ala Gln Met Glu Tyr Cys Arg  
 210 215 220

Thr Pro Cys Thr Val Ser Cys Asn Ile Pro Val Val Ser Gly Lys Glu  
 225 230 235 240

Cys Glu Glu Ile Ile Arg Lys Gly Gly Glu Thr Ser Glu Met Tyr Leu  
 245 250 255

Ile Gln Pro Asp Ser Ser Val Lys Pro Tyr Arg Val Tyr Cys Asp Met  
 260 265 270

Asn Thr Glu Asn Gly Gly Trp Thr Val Ile Gln Asn Arg Gln Asp Gly  
 275 280 285

Ser Val Asp Phe Gly Arg Lys Trp Asp Pro Tyr Lys Gln Gly Phe Gly  
 290 295 300

Asn Val Ala Thr Asn Thr Asp Gly Lys Asn Tyr Cys Gly Leu Pro Gly  
 305 310 315 320

Glu Tyr Trp Leu Gly Asn Asp Lys Ile Ser Gln Leu Thr Arg Met Gly  
 325 330 335

Pro Thr Glu Leu Leu Ile Glu Met Glu Asp Trp Lys Gly Asp Lys Val  
 340 345 350

Lys Ala His Tyr Gly Gly Phe Thr Val Gln Asn Glu Ala Asn Lys Tyr  
 355 360 365

Gln Ile Ser Val Asn Lys Tyr Arg Gly Thr Ala Gly Asn Ala Leu Met  
 370 375 380

Asp Gly Ala Ser Gln Leu Met Gly Glu Asn Arg Thr Met Thr Ile His  
 385 390 395 400

Asn Gly Met Phe Phe Ser Thr Tyr Asp Arg Asp Asn Asp Gly Trp Leu  
 405 410 415

Thr Ser Asp Pro Arg Lys Gln Cys Ser Lys Glu Asp Gly Gly Gly Trp  
 420 425 430

Trp Tyr Asn Arg Cys His Ala Ala Asn Pro Asn Gly Arg Tyr Tyr Trp  
 435 440 445

Gly Gly Gln Tyr Thr Trp Asp Met Ala Lys His Gly Thr Asp Asp Gly  
 450 455 460

Val Val Trp Met Asn Trp Lys Gly Ser Trp Tyr Ser Met Arg Lys Met

465 470 475 480

Ser Met Lys Ile Arg Pro Phe Phe Pro Gln Gln  
485 490

|       |                     |
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| <212> | PRT                 |
| <213> | Artificial sequence |

<220>  
<223> 99-5 immunogen

<400> 26

Met Glu Asp Ser Thr Thr Asn Ile Thr Lys His Gln Lys Trp Thr Val  
1 5 10 15

Glu Glu Ser Glu Trp Val Lys Ala Gly Val Gln Lys Tyr Gly Glu Gly  
20 25 30

Asn Trp Ala Ala Ile Ser Lys Asn Tyr Pro Phe Val Asn Arg Thr Ala

His Met Ile Lys His Arg Trp Arg His Met Lys Arg Leu Gly Met Asn  
50 55 60

Ser Gly Thr Asn Leu Val Pro Arg Gly Ser Gly Ile Glu Gly Arg Thr  
65 70 75 80

Met Ala Ile Ser Asp Pro Asn Ser Ser Ser Cys Asn Ile Pro Val Val  
85 90 95

Ser Gly Lys Glu Cys Glu  
100

|       |                     |
|-------|---------------------|
| <210> | 27                  |
| <211> | 265                 |
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| <213> | Artificial Sequence |

<220>  
<223> 1101 iimunogen

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Met Thr Val Ser Cys Asn Ile Pro Val Val Ser Gly Lys Glu Cys Glu  
1 5 10 15

Glu Ile Ile Arg Lys Gly Gly Glu Thr Ser Glu Met Tyr Leu Ile Gln  
20 25 30

Pro Asp Ser Ser Val Lys Pro Tyr Arg Val Tyr Cys Asp Met Asn Thr  
35 40 45

Glu Asn Gly Gly Trp Thr Val Ile Gln Asn Arg Gln Asp Gly Ser Val  
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60

50

55

Asp Phe Gly Arg Lys Trp Asp Pro Tyr Lys Gln Gly Phe Gly Asn Val  
65 70 75 80

Ala Thr Asn Thr Asp Gly Lys Asn Tyr Cys Gly Leu Pro Gly Glu Tyr  
85 90 95

Trp Leu Gly Asn Asp Lys Ile Ser Gln Leu Thr Arg Met Gly Pro Thr  
100 105 110

Glu Leu Leu Ile Glu Met Glu Asp Trp Lys Gly Asp Lys Val Lys Ala  
115 120 125

His Tyr Gly Gly Phe Thr Val Gln Asn Glu Ala Asn Lys Tyr Gln Ile  
130 135 140

Ser Val Asn Lys Tyr Arg Gly Thr Ala Gly Asn Ala Leu Met Asp Gly  
145 150 155 160

Ala Ser Gln Leu Met Gly Glu Asn Arg Thr Met Thr Ile His Asn Gly  
165 170 175

Met Phe Phe Ser Thr Tyr Asp Arg Asp Asn Asp Gly Trp Leu Thr Ser  
180 185 190

Asp Pro Arg Lys Gln Cys Ser Lys Glu Asp Gly Gly Gly Trp Trp Tyr  
195 200 205

Asn Arg Cys His Ala Ala Asn Pro Asn Gly Arg Tyr Tyr Trp Gly Gly  
210 215 220

Gln Tyr Thr Trp Asp Met Ala Lys His Gly Thr Asp Asp Gly Val Val  
225 230 235 240

Trp Met Asn Trp Lys Gly Ser Trp Tyr Ser Met Arg Lys Met Ser Met  
245 250 255

Lys Ile Arg Pro Phe Phe Pro Gln Gln  
260 265

<210> 28  
<211> 12  
<212> PRT  
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<220>  
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<400> 28

Cys Asn Ile Pro Val Val Ser Gly Lys Glu Cys Glu  
1 5 10