<110> HANMI PHARM. CO., LTD.

<120> USE OF A LONG ACTING GLP-1/GLUCAGON RECEPTOR DUAL AGONIST FOR THE TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE

<130> OPA15087-PCT

<150> KR 10-2014-0122862
<151> 2014-09-16

<160> 34

<170> KopatentIn 2.0

<210> 1
<211> 37
<212> PRT
<213> Homo sapiens

<220>
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<400> 1
His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

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<220>
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<220>
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<400> 2
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

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<220>
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<400> 3
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Ala Trp Leu Lys Asn Thr Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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<223> Xaa = 4-imidazoacetyl

<400> 4
Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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<220>
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<222> (1)
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<400> 5
Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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<400> 6
Xaa Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Arg Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Ala Ala His Ser Gln Gly Thr
20 25 30

Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp
35 40

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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Met Asn Thr Lys
20 25 30

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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Leu Ser Arg Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Met Asn Lys
20 25

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<223> Xaa = 4-imidazoacetyl

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<222> (20)
<223> Xaa = alpha-methyl glutamic acid

<400> 9
Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Xaa Leu Phe Ile Glu Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

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<400> 10
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Met Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser Lys
35 40

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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Ala Ala His Ser Gln Gly Thr
20 25 30

Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Lys
35 40

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<400> 12
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Gly
1 5 10 15

Gly Gly His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met
20 25 30

Glu Glu Glu Ala Val Lys
35

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<223> Xaa = 4-imidazoacetyl

<220>
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<222> (16)
<223> Xaa = alpha-methyl-glutamic acid

<220>
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<222> (20)
<223> Xaa = alpha-methyl-glutamic acid

<400> 13
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1 5 10 15

Glu Ala Val Xaa Leu Phe Ile Glu Trp Leu Met Asn Thr Lys
20 25 30

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<223> Xaa = alpha-methyl-glutamic acid

<220>
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<222> (24)
<223> Xaa = alpha-methyl-glutamic acid

<400> 14
Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Xaa Leu Phe Ile Xaa Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

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<220>
<221> VARIANT
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<222> (24)
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<400> 15
Xaa Gly Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Xaa Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

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<220>
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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Leu Ser Arg Gln Leu Glu Gly
 1   5   10   15

Gly Gly His Ser Gln Gly Thr Phe Thr Ser Asp Leu Ser Arg Gln Leu
            20   25   30

Glu Lys

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<400> 17
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
 1   5   10   15

Glu Ala Val Arg Leu Phe Ile Glu Trp Ile Arg Asn Thr Lys Arg Asn
            20   25   30

Arg Asn Asn Ile Ala
        35

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<223> Xaa = 4-imidazoacetyl

<400> 18
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu

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  1               5                  10                  15

Glu Ala Val Arg Leu Phe Ile Glu Trp Ile Arg Asn Gly Gly Pro Ser
            20                  25                  30

Ser Gly Ala Pro Pro Pro Ser Lys
         35                  40


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<220>
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<400>    19
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
  1               5                  10                  15

Glu Ala Val Lys Leu Phe Ile Glu Trp Ile Arg Asn Thr Lys Arg Asn
            20                  25                  30

Arg Asn Asn Ile Ala
         35


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<223>    Xaa = 4-imidazoacetyl


<400>    20
Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Tyr Leu Asp Glu
  1               5                  10                  15

Glu Ala Val Lys Leu Phe Ile Glu Trp Ile Arg Asn Gly Gly Pro Ser
            20                  25                  30

Ser Gly Ala Pro Pro Pro Ser Lys
         35                  40


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<223>    oxyntomodulin derivative

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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Arg Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Val Arg Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

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<220>
<221> VARIANT
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<223> Xaa = desamino-histidyl

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Xaa Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Lys
20 25 30

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<223> Xaa = aminoisobutyric acid

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His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Cys Trp Leu Met Asn Thr
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His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
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<220>
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<223> Xaa = aminoisobutyric acid

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His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30

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Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30

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<222> (2)
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Gln Ala Ala Lys Glu Phe Ile Cys Trp Leu Met Asn Thr
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1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr
20 25

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<222> (2)
<223> Xaa = d-serine

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His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

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1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

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<223> Xaa = 4-imidazoacetyl

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<222> (2)
<223> Xaa = d-serine

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Xaa Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

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<223> Xaa = aminoisobutyric acid

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Xaa Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30

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<400> 33
His Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ala Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30

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Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Glu
1 5 10 15

Lys Arg Ala Lys Glu Phe Val Gln Trp Leu Met Asn Thr Cys
20 25 30