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(73)	Proprietor	Novo Nordisk A/S, Novo Allé, 2880 Bagsværd, Danmark
(72)	Inventor	ØSTERGAARD, Søren, Novo Allé, DK-2880 Bagsværd, Danmark FRIEBOES, Kilian Waldemar Conde, Novo Allé, DK-2880 Bagsværd, Danmark WIECZOREK, Birgit, Novo Allé, DK-2880 Bagsværd, Danmark THOMSEN, Jens Kaalby, Novo Allé, DK-2880 Bagsværd, Danmark WULFF, Birgitte Schjellerup, Novo Allé, DK-2880 Bagsværd, Danmark JESSEN, Carsten, Novo Allé, DK-2880 Bagsværd, Danmark
(74)	Agent or Attorney	VENI GmbH, Villa de Meuron, Buristrasse 21, 3006 BERN, Sveits

(54) Title **SELECTIVE PYY COMPOUNDS AND USES THEREOF**

(56) References Cited:

EP-A1- 2 992 008, WO-A1-2009/033710, WO-A2-2010/052144, WO-A1-2010/031707, WO-A1-2011/033068

SØREN L. PEDERSEN ET AL: "Peptide hormone isoforms: N-terminally branched PYY3-36 isoforms give improved lipid and fat-cell metabolism in diet-induced obese mice", JOURNAL OF PEPTIDE SCIENCE, vol. 16, no. 11, 1 November 2010 (2010-11-01), pages 664-673, XP055057989, ISSN: 1075-2617, DOI: 10.1002/psc.1281

ROGER REIDELBERGER ET AL: "Effects of glycine-extended and serine-phosphorylated forms of peptide YY on food intake in rats", PEPTIDES, ELSEVIER, AMSTERDAM, NL, vol. 32, no. 4, 2 January 2011 (2011-01-02), pages 770-775, XP028210544, ISSN: 0196-9781, DOI: 10.1016/J.PEPTIDES.2011.01.005 [retrieved on 2011-01-22]

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (http://worldwide.espacenet.com) or via the search engine on our website here: https://search.patentstyret.no/

PATENTKRAV

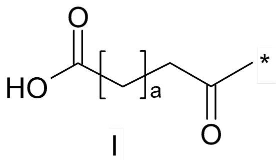
1. PYY-forbindelse som er i stand til å binde til den humane Y2-reseptoren som omfatter

i) tryptofan i posisjonen som tilsvarer posisjon 30 i hPYY(1-36),

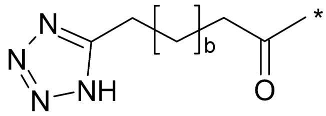
ii) N(alfa)-metyl-L-arginin i en posisjon som tilsvarer posisjon 35 i hPYY(1-36),

iii) lysin i en posisjon som tilsvarer posisjon 7 i hPYY(1-36) og en modifiserende gruppe festet til epsilonaminogruppen av lysinet, hvori den modifiserende gruppen defineres av **A-B-C-,**

hvori **A-** er valgt fra


I

,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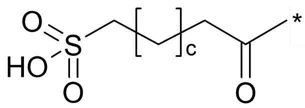
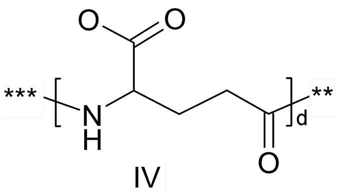

III

,

hvori a er et heltall fra 12 til 19, b er et heltall fra 10 til 16, og c er et heltall fra 10 til 16, og hvori * betegner festepunktet til –B-,

hvori **B-** er valgt fra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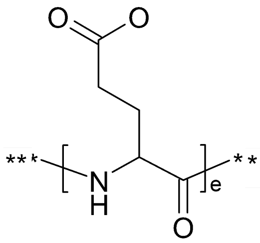
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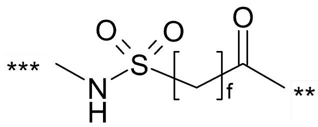
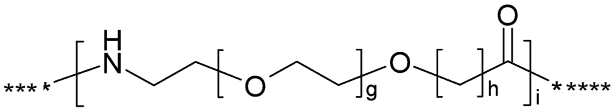

VI

hvori d er 1 eller 2; e er 1 eller 2; og f er 2, 3 eller 4; og hvori *** betegner festepunktet til A-, og ** betegner festepunktet til –C-,

hvori **-C-** er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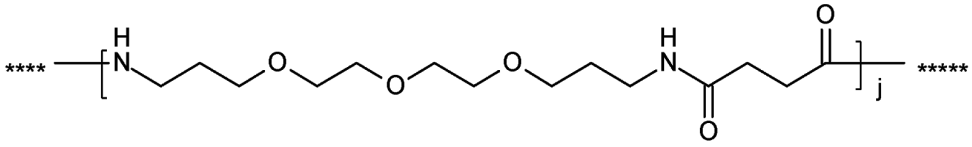


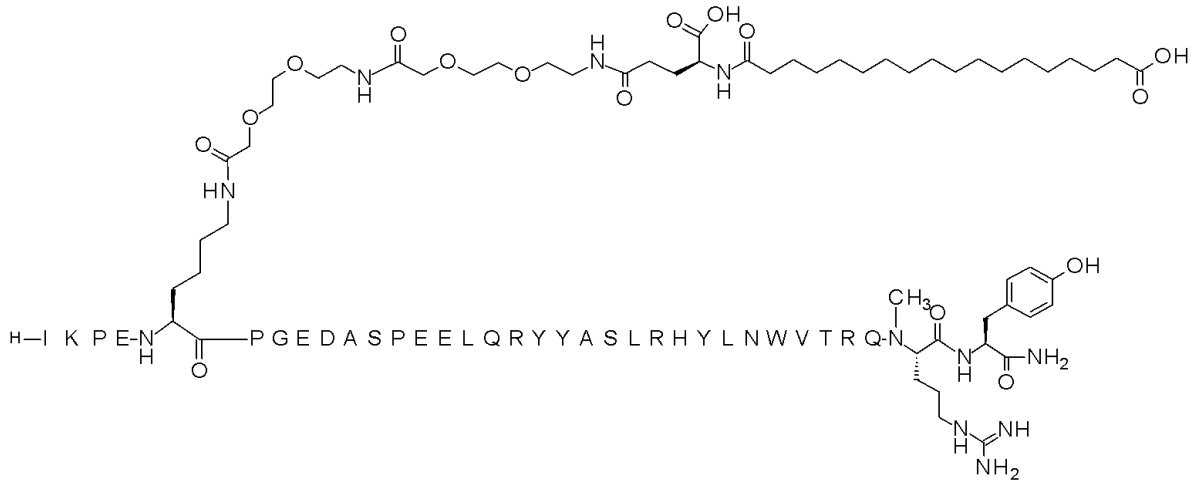
VIII ,

hvori g er et heltall i området fra 1-5, h er et heltall i området fra 1-5, i er et heltall i området fra 2 til 6, j er et heltall i området fra 1 til 6, og hvori **** betegner festepunktet til -B- og ***** betegner festepunktet til epsilonaminogruppen av lysinresten i posisjonen som tilsvarer posisjon 7 i hPYY(1-36),
og maksimalt 8 aminosyremodifikasjoner sammenlignet med hPYY(3-36), eller et farmasøytisk akseptabelt salt derav.

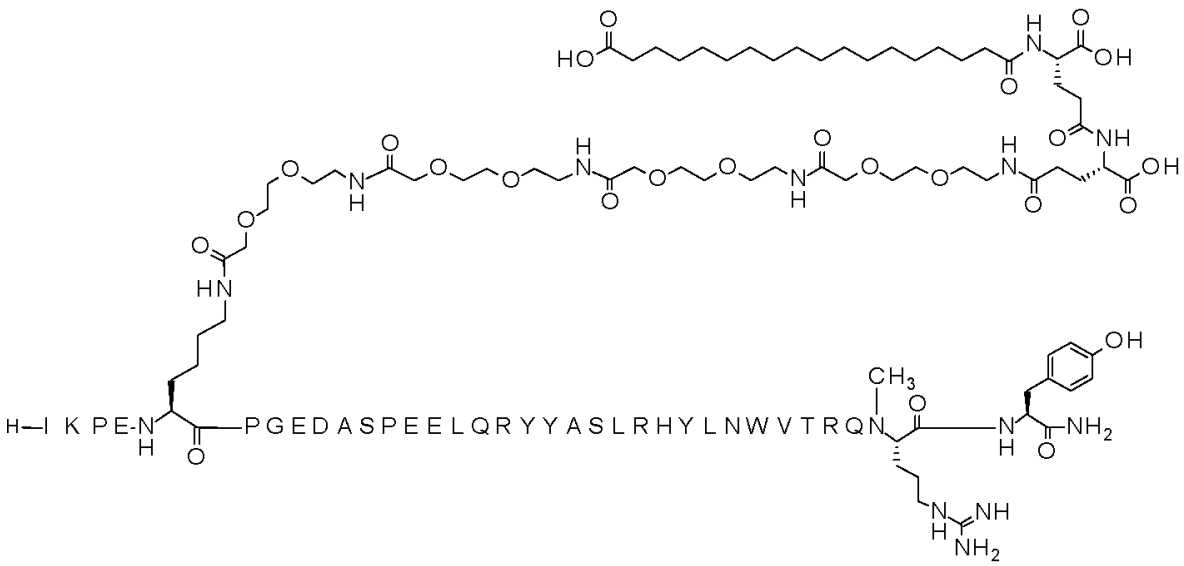
2. PYY-forbindelsen ifølge krav 1, hvori PYY-forbindelsen omfatter glutamin i en posisjon som tilsvarer posisjon 18 i hPYY(1-36).

3. PYY-forbindelse ifølge et hvilket som helst av kravene 1-2 valgt fra følgende:

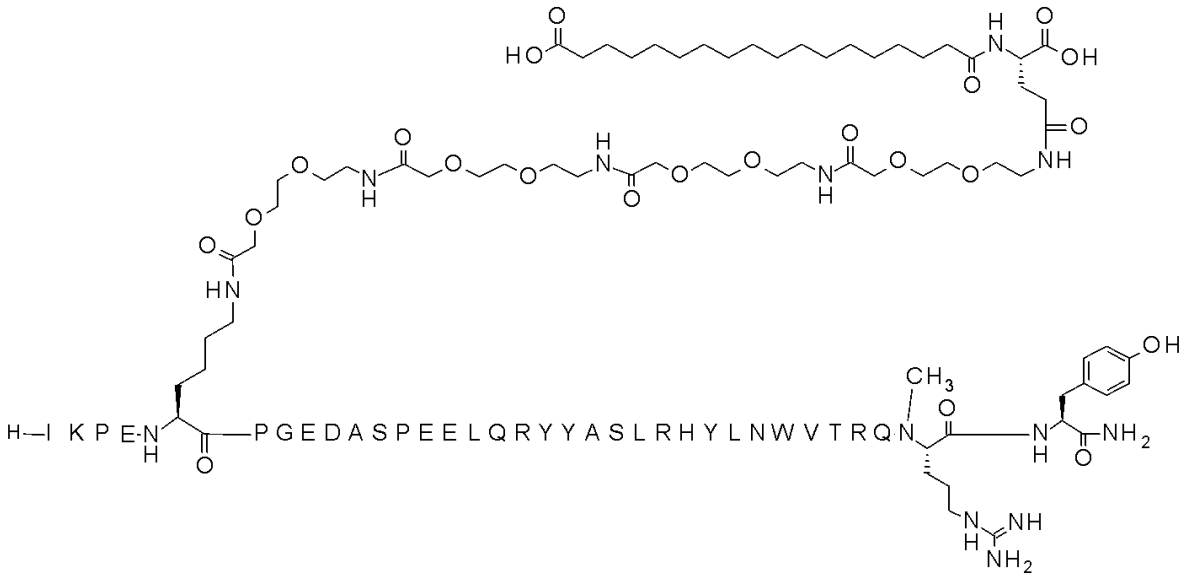
7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(17-karboksyheptadekanoylamino)-
butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]-[Lys7,Gln18, Trp30,NMeArg35]hPYY(3-36) (SEQ ID NO:5)



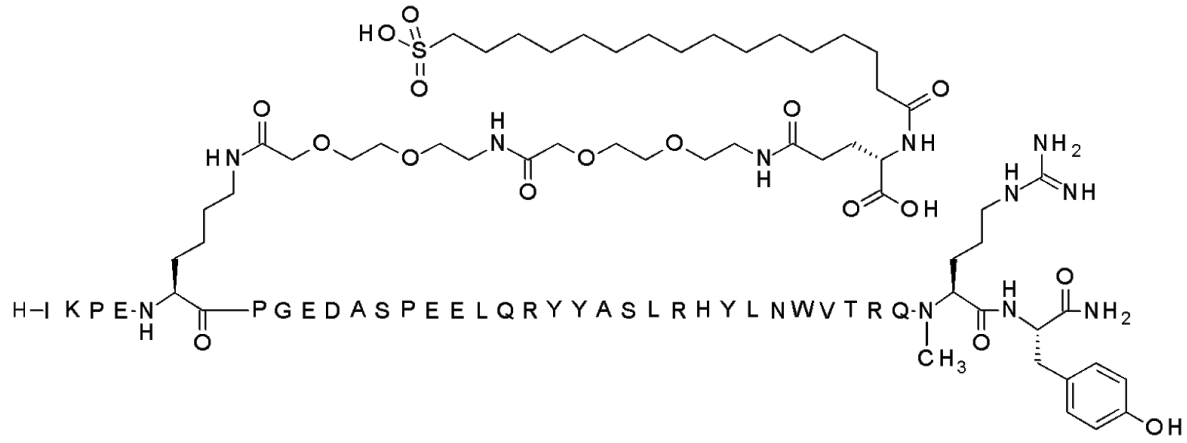
7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-[[(4S)-4-karboksy-4-(17-karboksyheptadekanoylamino)butanoyl]amino]butanoyl]amino]-
etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]amino]-
etoksy]etoksy]acetyl]-[Lys7,Gln18,Trp30,NMeArg35]hPYY(3-36) (SEQ ID NO:6)



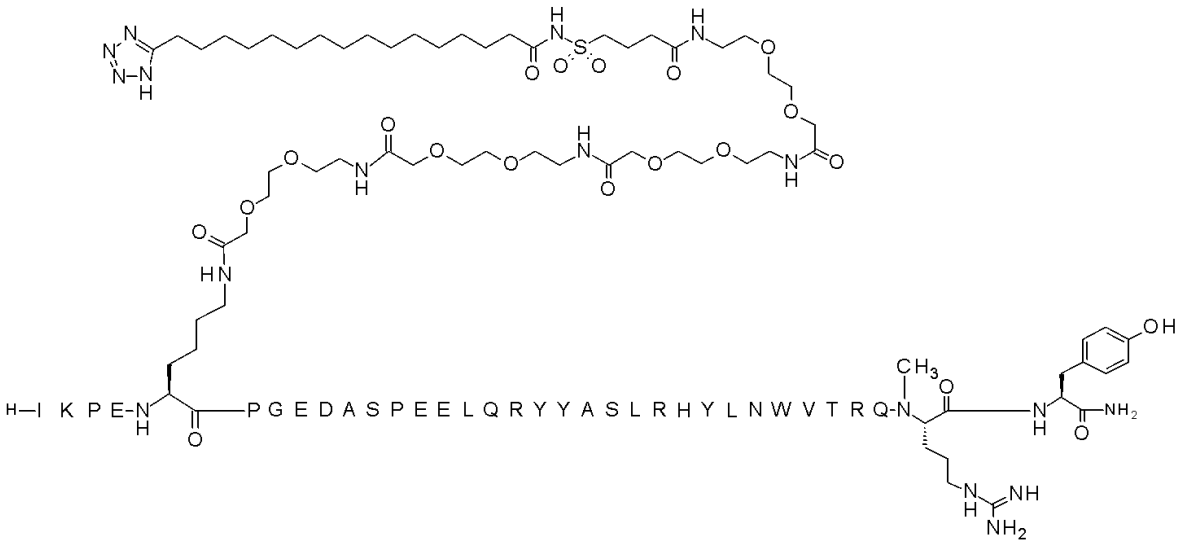
7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(17-karboksyheptadekanoylamino)butanoyl]amino]etoksy]etoksy]acetyl]amino]-
etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]-[Lys7,Gln18,Trp30,NMeArg35]hPYY(3-36) (SEQ ID NO:7)



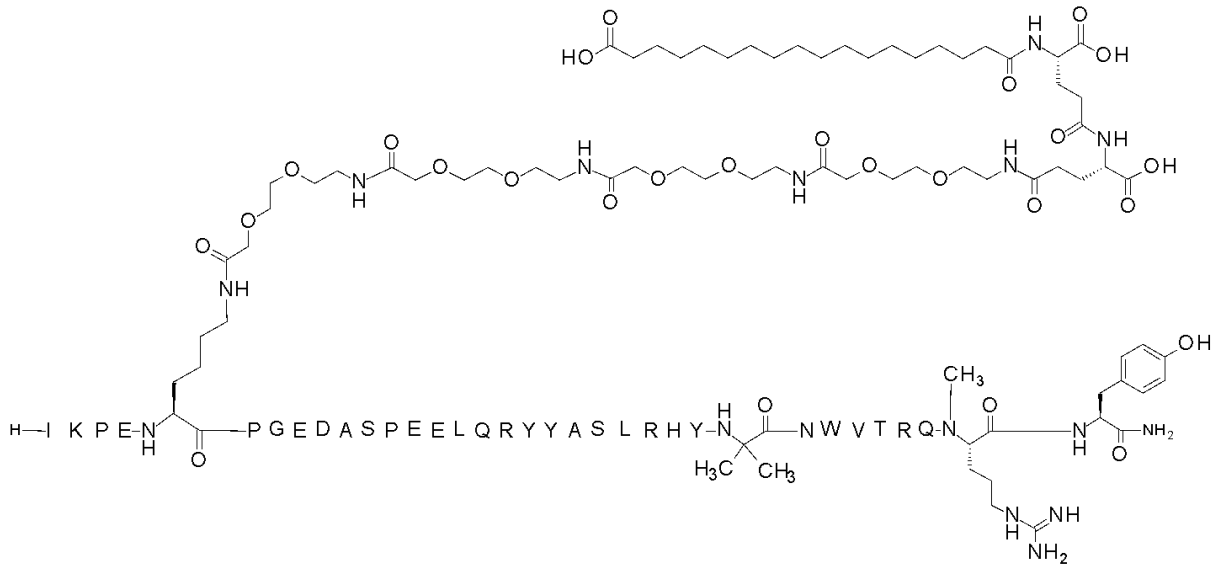
7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)-
butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]-[Lys7,Gln18,Trp30, NMeArg35]hPYY(3-36) (SEQ ID NO:8)



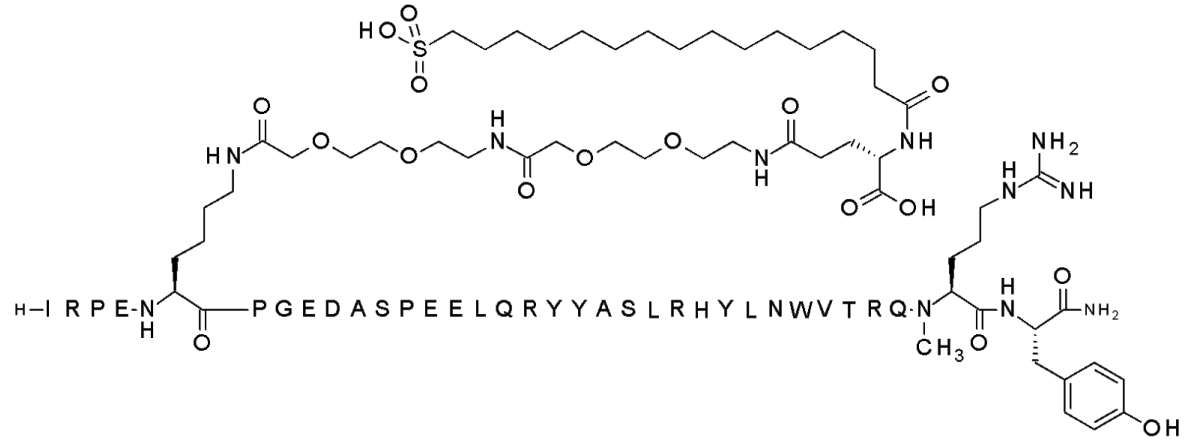
7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[4-[16-(1H-tetrazol-5-yl)-heksadekanoylsulfamoyl]butanoylamino]etoksy]etoksy]acetyl]amino]etoksy]-etoksy]acetyl]amino]etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]-[Lys7,Gln18, Trp30,NMeArg35]hPYY(3-36) (SEQ ID NO:9)



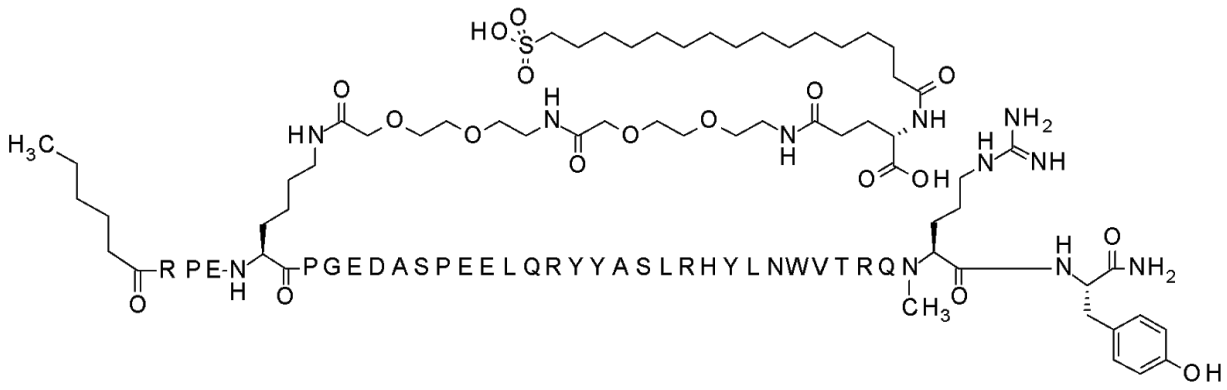
7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-[[(4S)-4-karboksy-4-(17-karboksyheptadekanoylamino)butanoyl]amino]butanoyl]-amino]etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]amino]etoksy]-etoksy]acetyl]amino]etoksy]etoksy]acetyl]-[Lys7,Gln18,Aib28,Trp30,NMeArg35] hPYY(3-36) (SEQ ID NO:10)



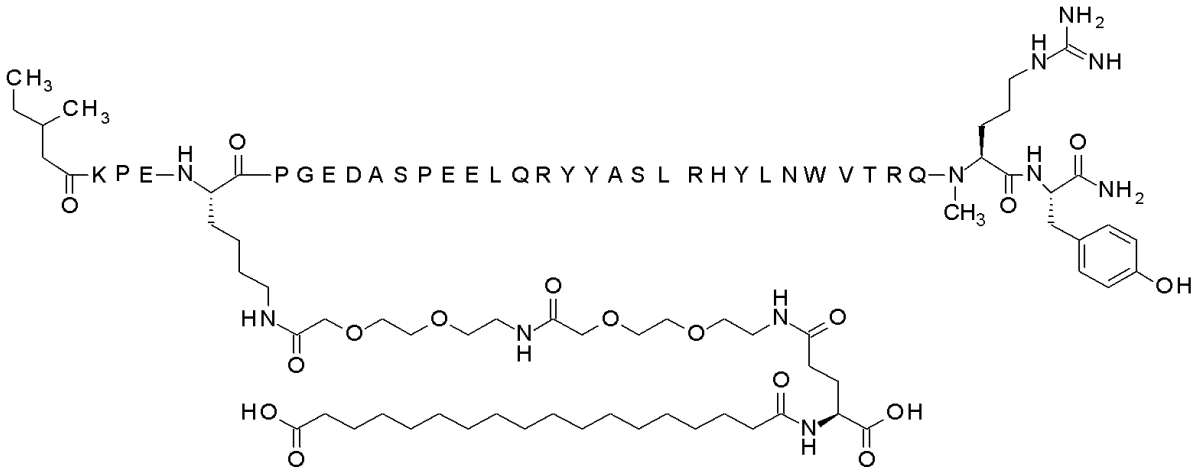
7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)-butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]-[Arg4,Lys7,Gln18, Trp30,NMeArg35]hPYY(3-36) (SEQ ID NO:11)



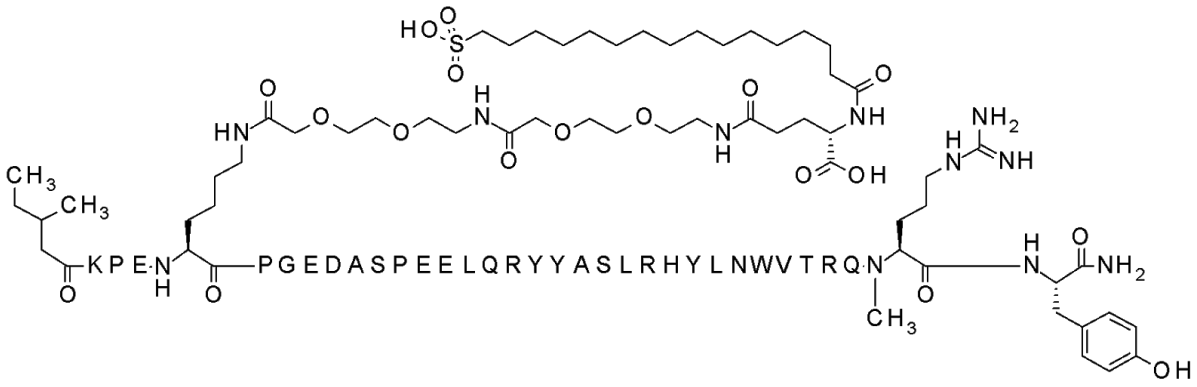
4-N{alfa}-(heksanoyl)-7-N{Epsilon}-2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]-etoksy]acetyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:12)



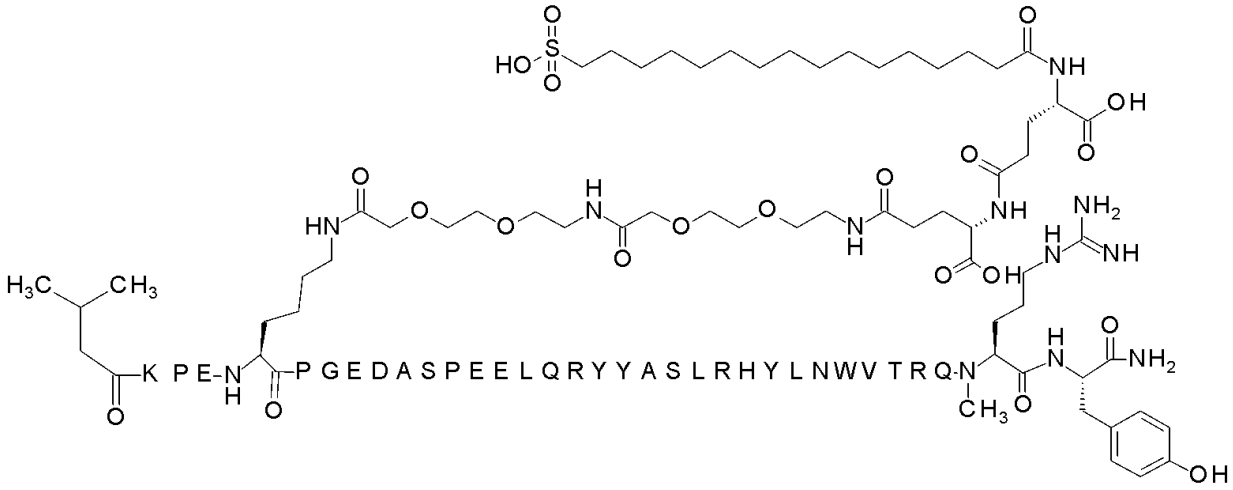
4-N{alfa}-(3-metyl-pentanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(17-karboksyheptadekanoylamino)butanoyl]amino]etoksy]etoksy]acetyl]amino]-etoksy]etoksy]acetyl]-[Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:13)



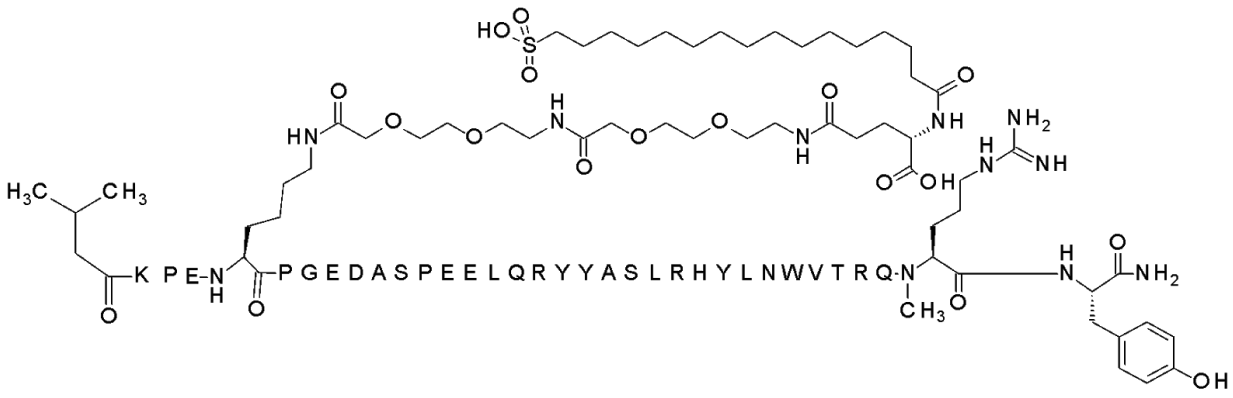
4-N{alfa}-(3-metyl-pentanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]etoksy]etoksy]acetyl]amino]-etoksy]etoksy]acetyl]-[Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:14)



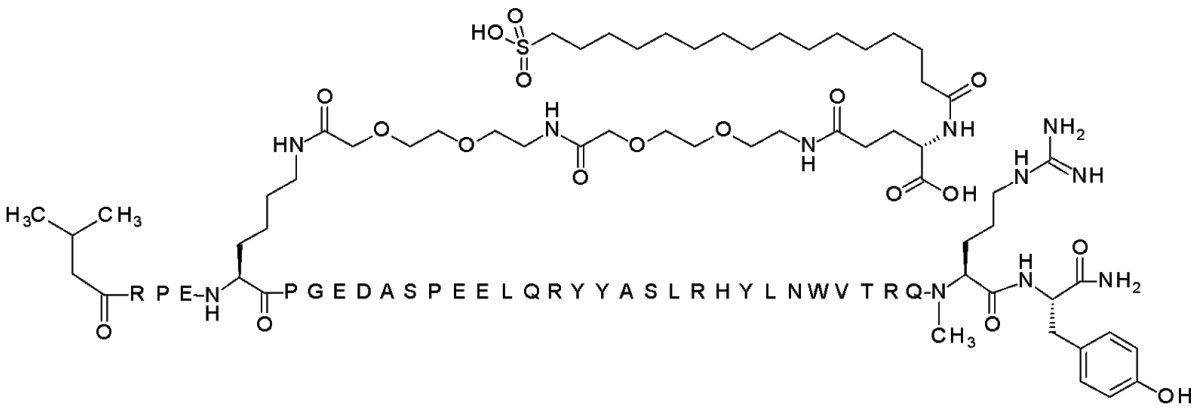
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]butanoyl]amino]-etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]-[Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:15)



4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]etoksy]etoksy]acetyl]amino]-etoksy]etoksy]acetyl]-[Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:16)



4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)-butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]-etoksy]acetyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:18)



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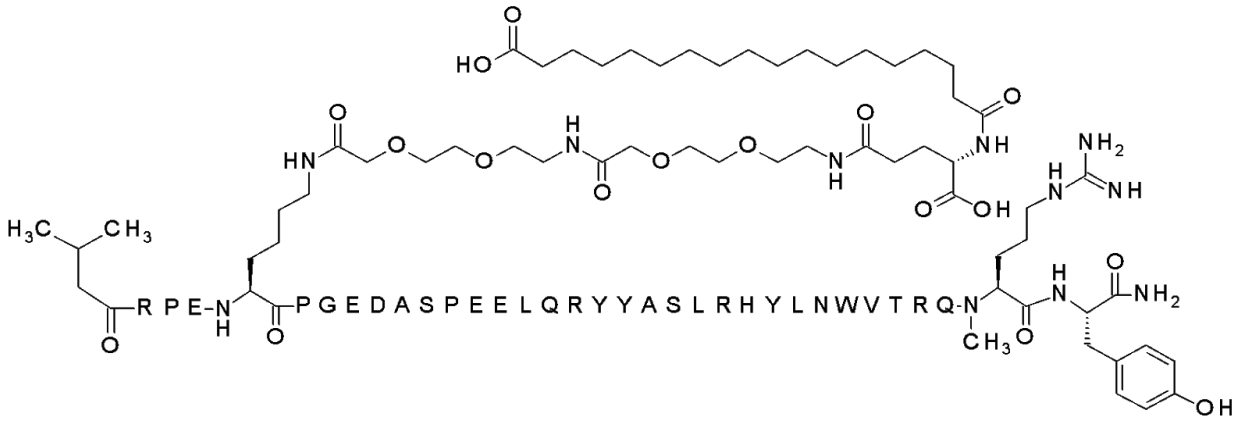
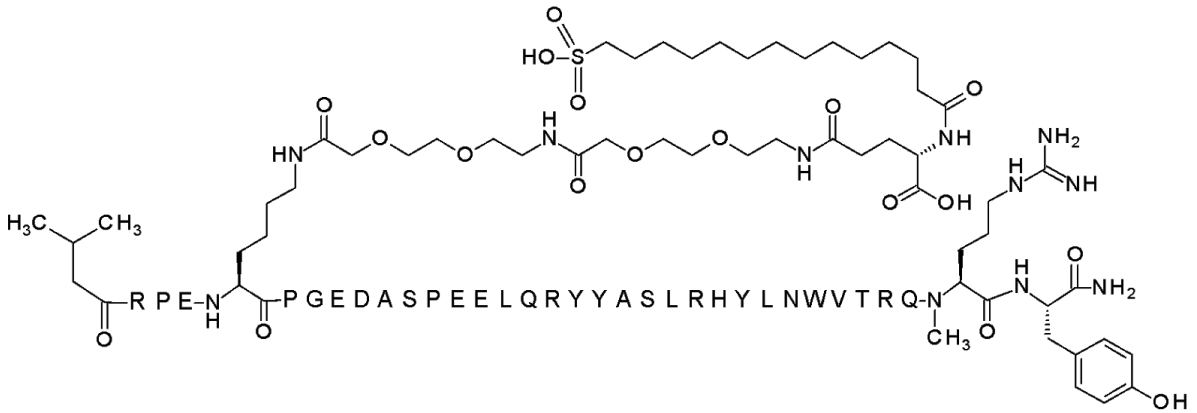


4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(14-sulfotetradekanoylamino)butanoyl]amino]etoksy]etoksy]acetyl]]amino]etoksy]-etoksy]acetyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:20)



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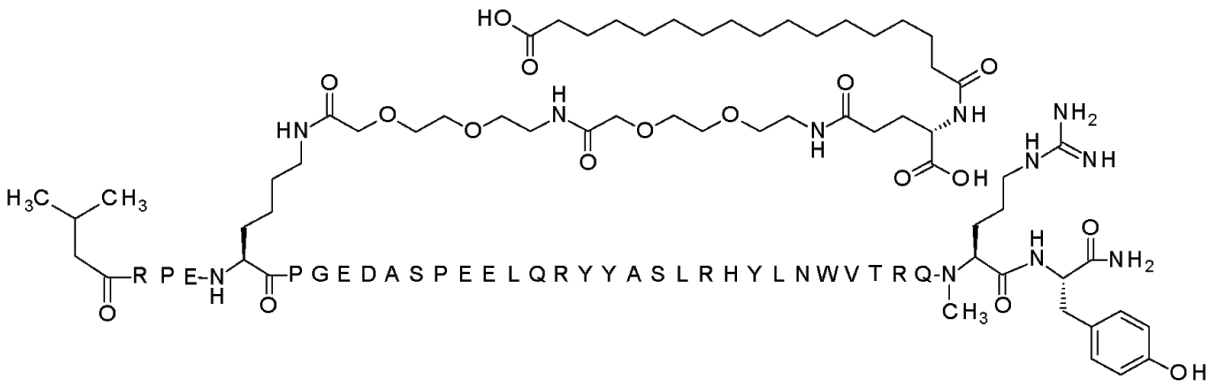

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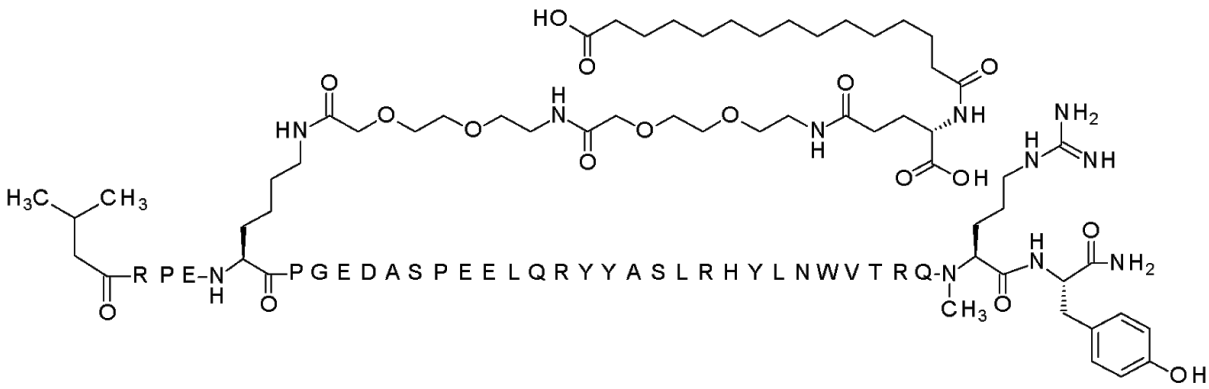

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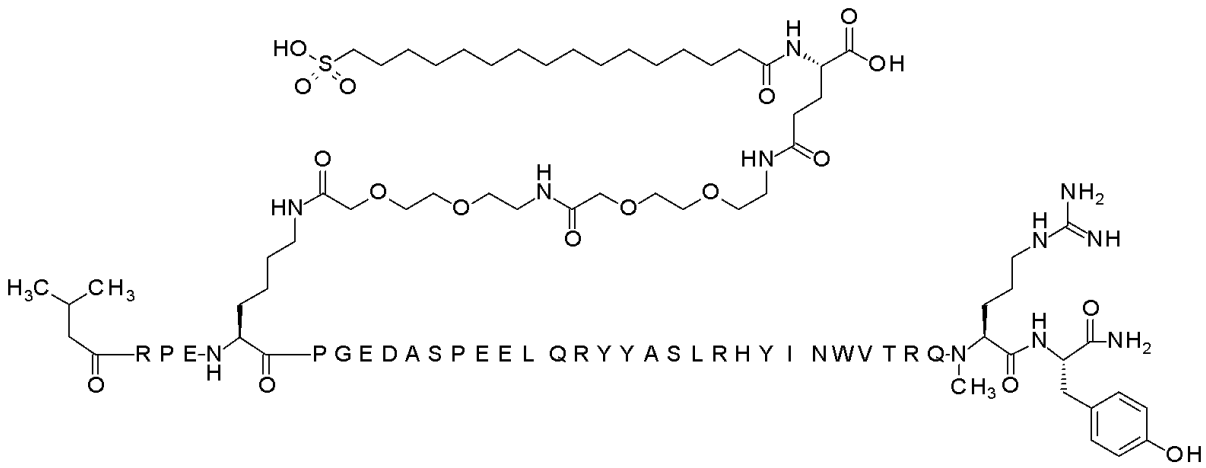

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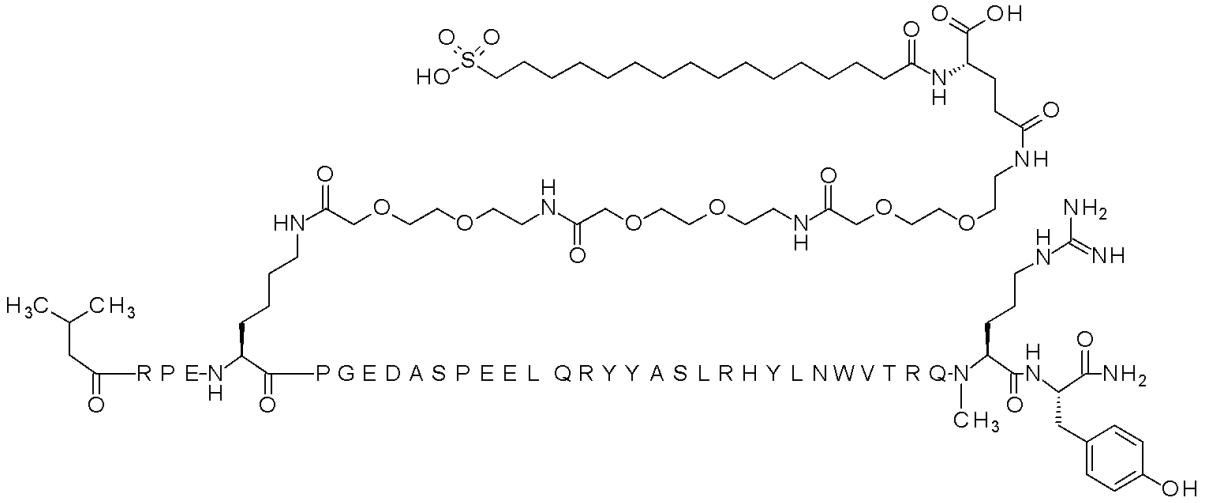

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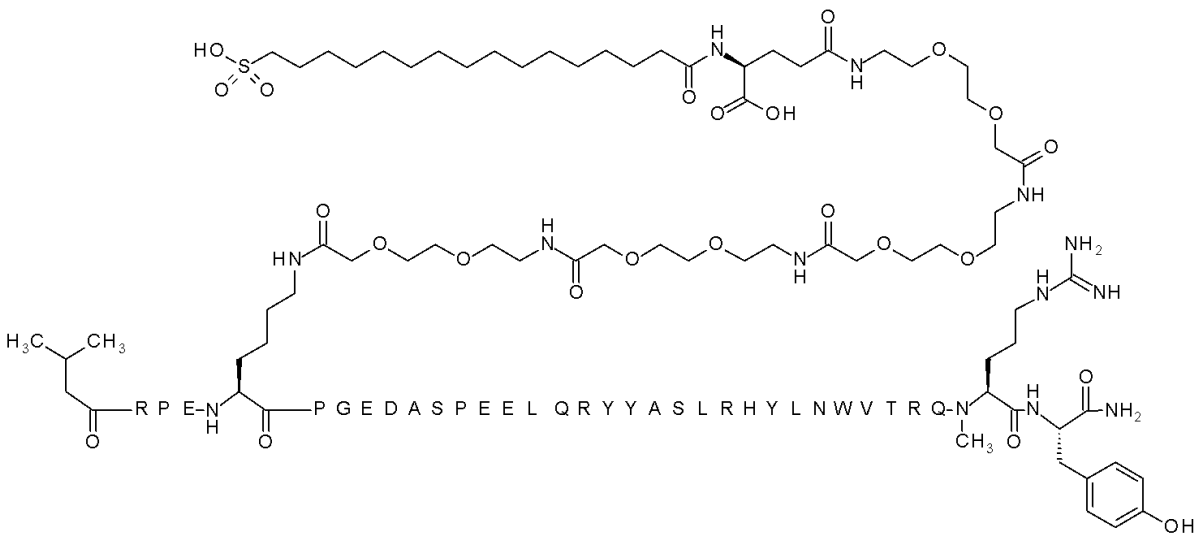
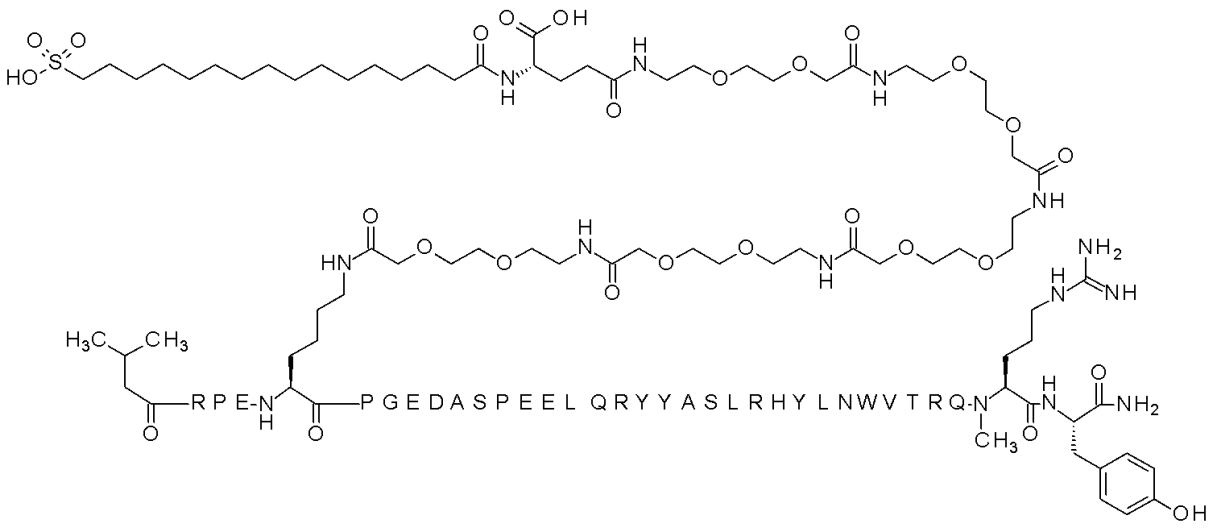
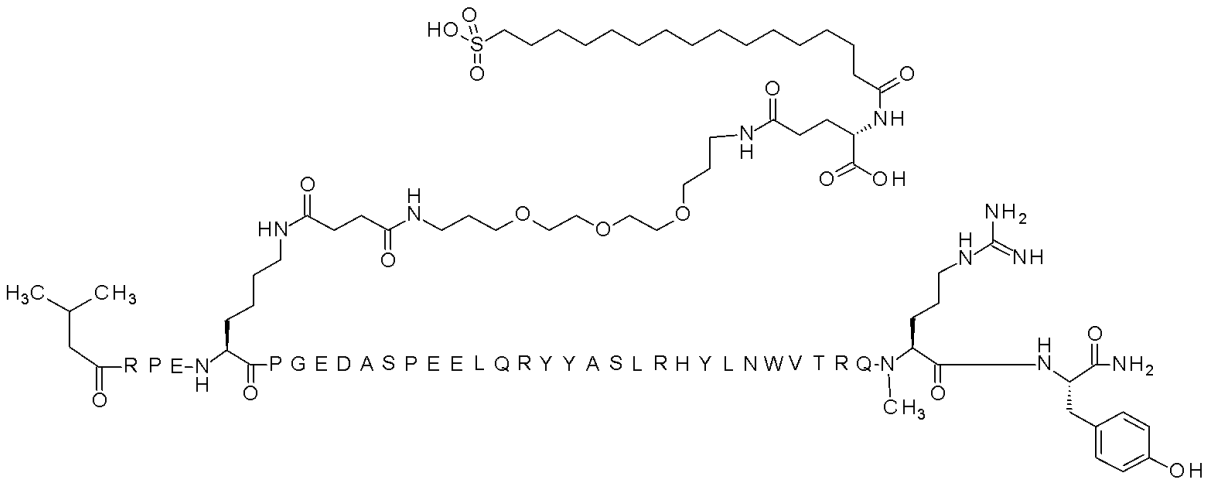


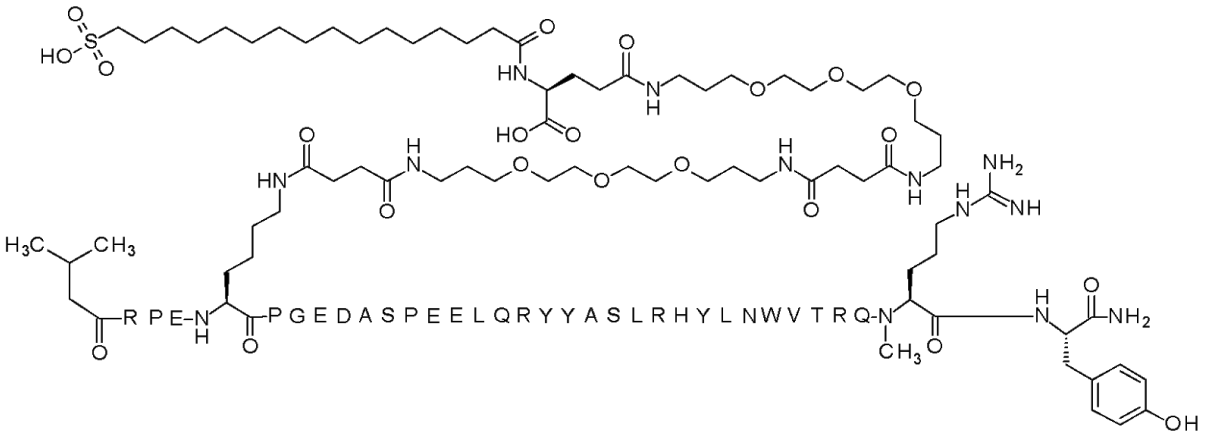
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]-etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]amino]-etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:26)



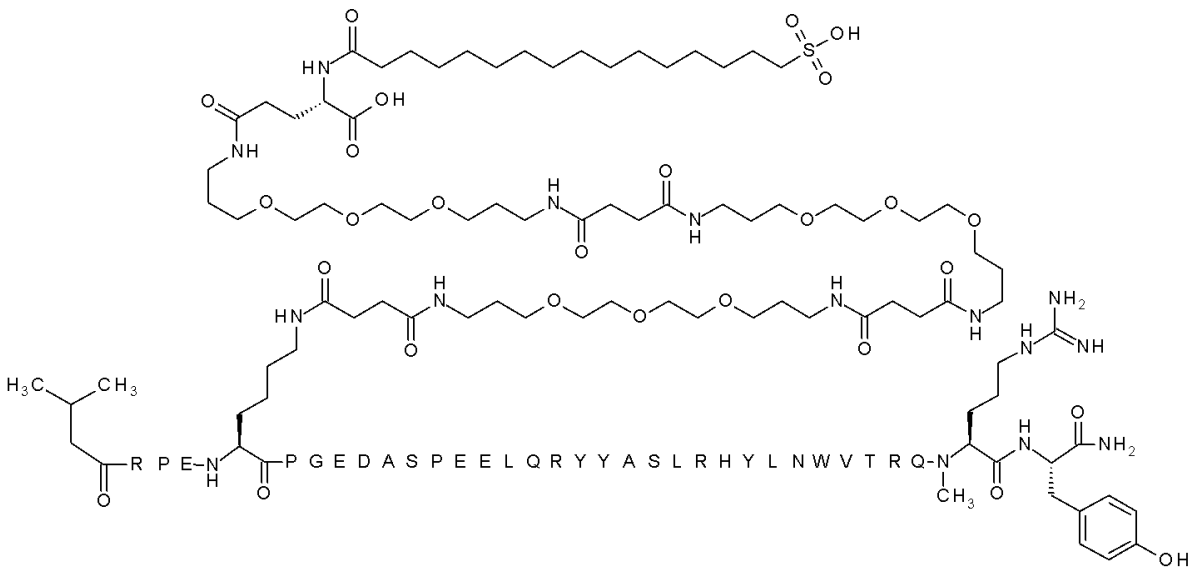
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[4-[3-[2-[2-[3-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]propoksy]etoksy]etoksy]propylamino]--oksobutanoyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:27)



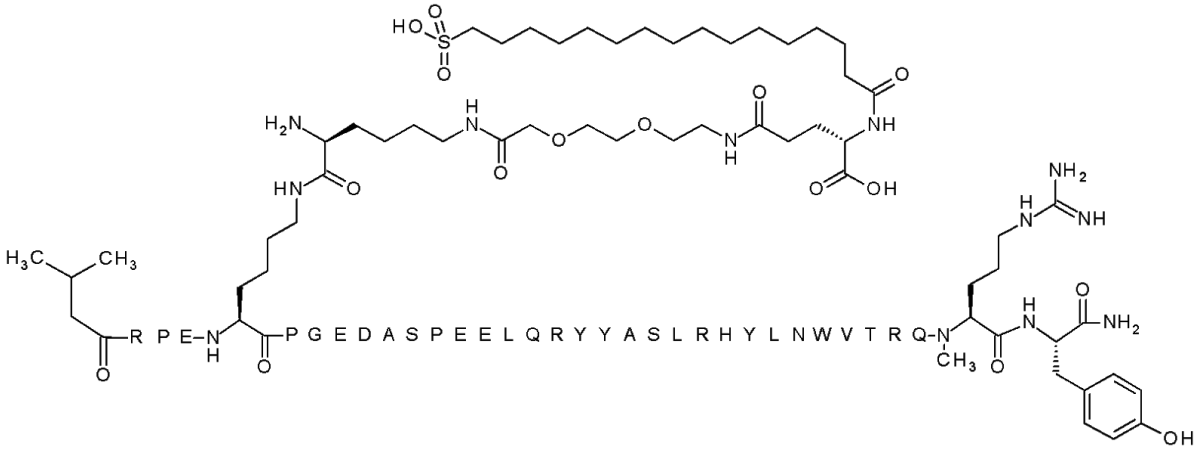
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[4-[3-[2-[2-[3-[[4-[3-[2-[2-[3-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]propoksy]etoksy]-etoksy]propylamino]-4-oksobutanoyl]amino]propoksy]etoksy]etoksy]propylamino]-4-oksobutanoyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:28)



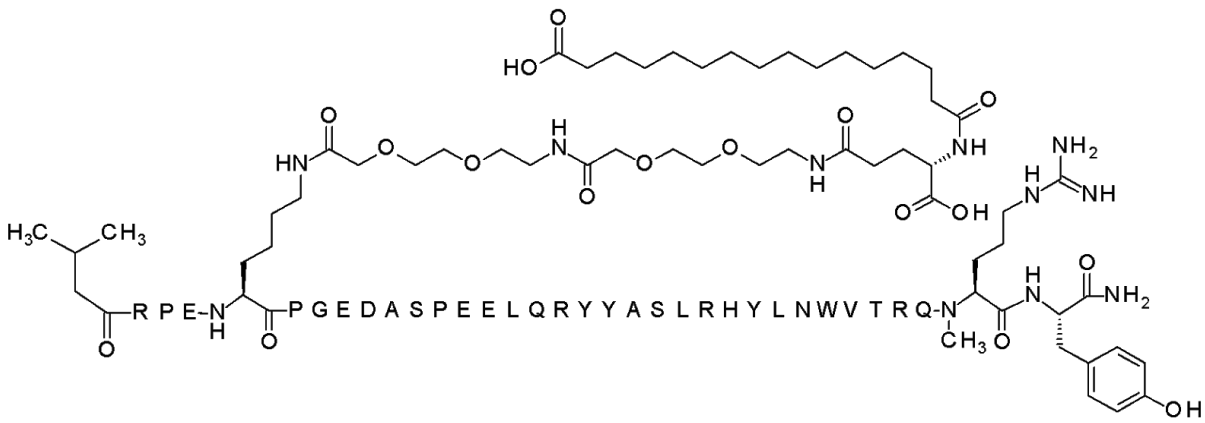
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[4-[3-[2-[2-[3-[[4-[3-[2-[2-[3-[[4-[3-[2-[2-[3-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]propoksy]-etoksy]etoksy]propylamino]-4-oksobutanoyl]amino]propoksy]etoksy]-etoksy]propylamino]-4-oksobutanoyl]amino]propoksy]etoksy]etoksy]propylamino]-4-oksobutanoyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:29)



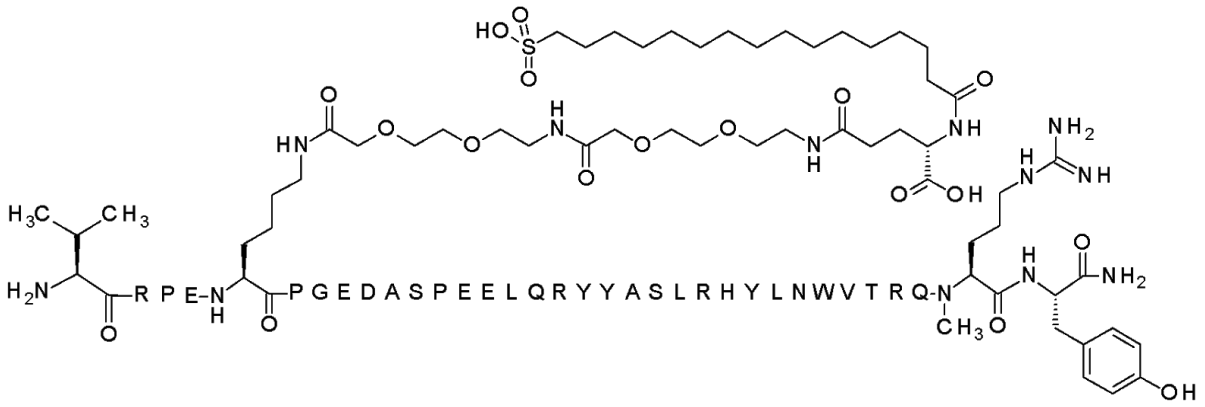
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[(2S)-2-amino-6-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]etoksy]etoksy]acetyl]-amino]heksanoyl]]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:30)



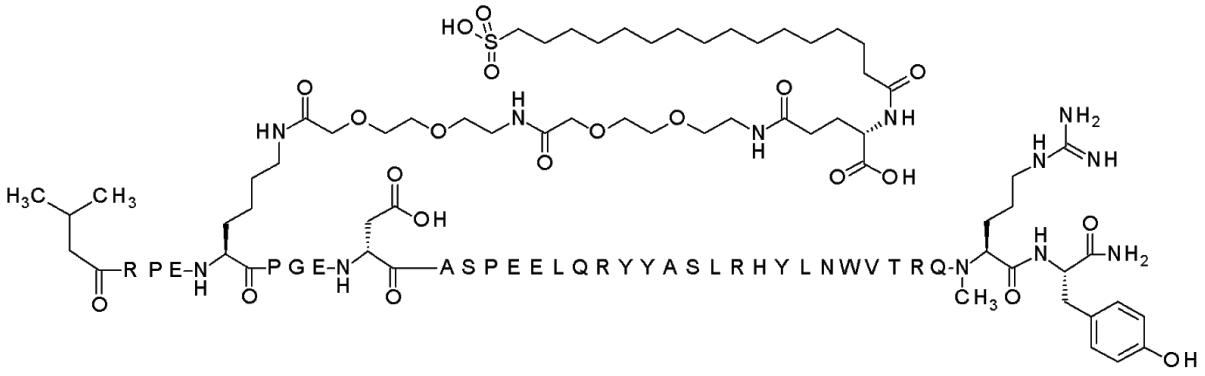
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(15-karboksypentadekanoylamino)butanoyl]amino]etoksy]etoksy]acetyl]amino]-etoksy]etoksy]acetyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:31)



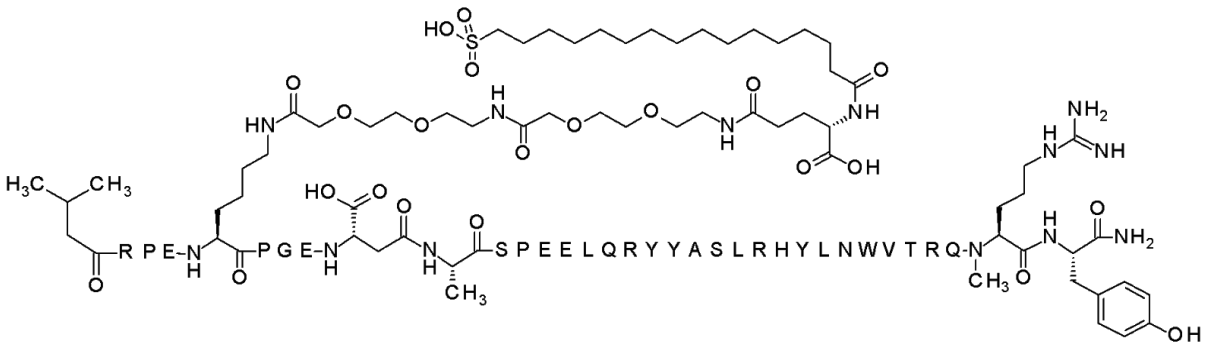
7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)-butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]-etoksy]acetyl]-[Val3,Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(3-36) (SEQ ID NO:32)



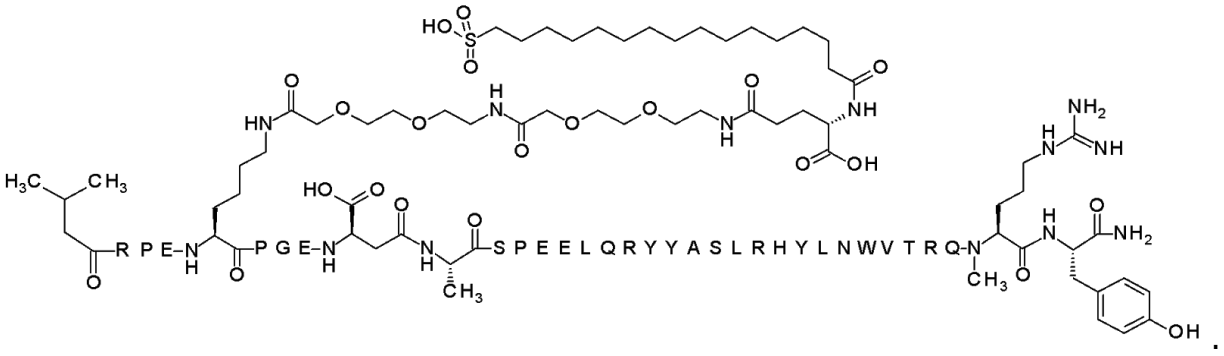
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)-butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]-etoksy]acetyl]-[Arg4,Lys7,D-Asp11,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:33)



4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)-butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]-etoksy]acetyl]-[Arg4,Lys7,isoAsp11,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:34)

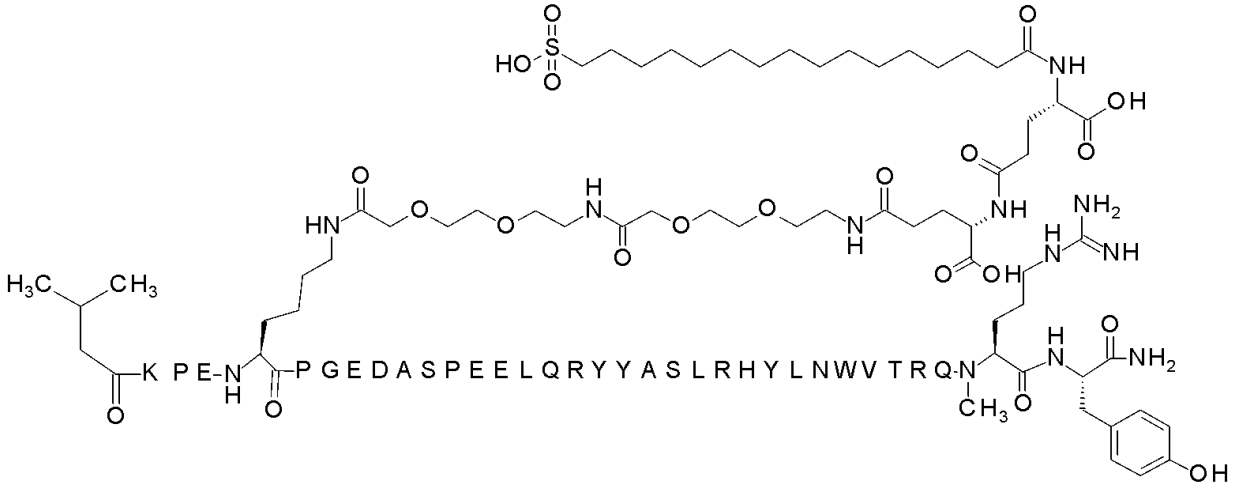


4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)-butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]-etoksy]acetyl]-[Arg4,Lys7,D-isoAsp11,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:35)



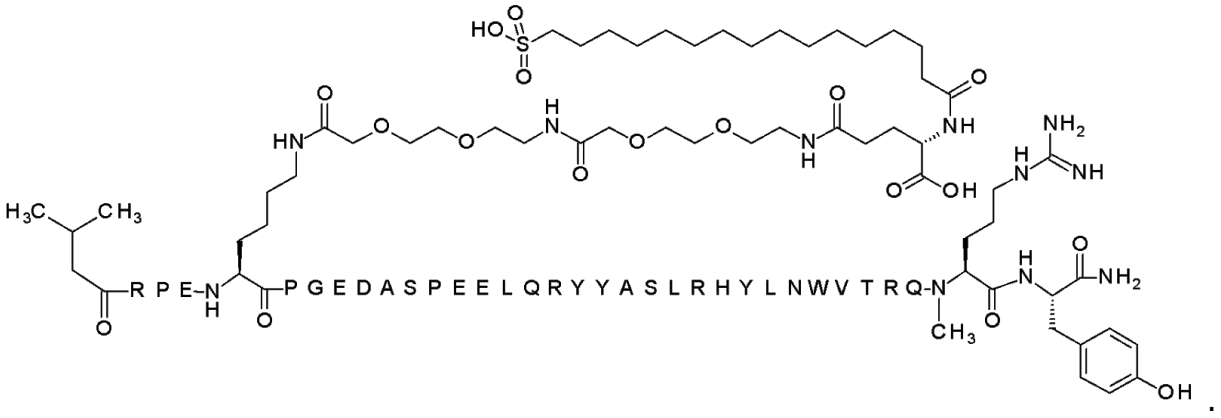
.

4. PYY-forbindelsen ifølge et hvilket som helst av de foregående kravene, hvori PYY-forbindelsen er
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]butanoyl]amino]-etoksy]etoksy]acetyl]amino]etoksy]etoksy]acetyl]-[Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:15)

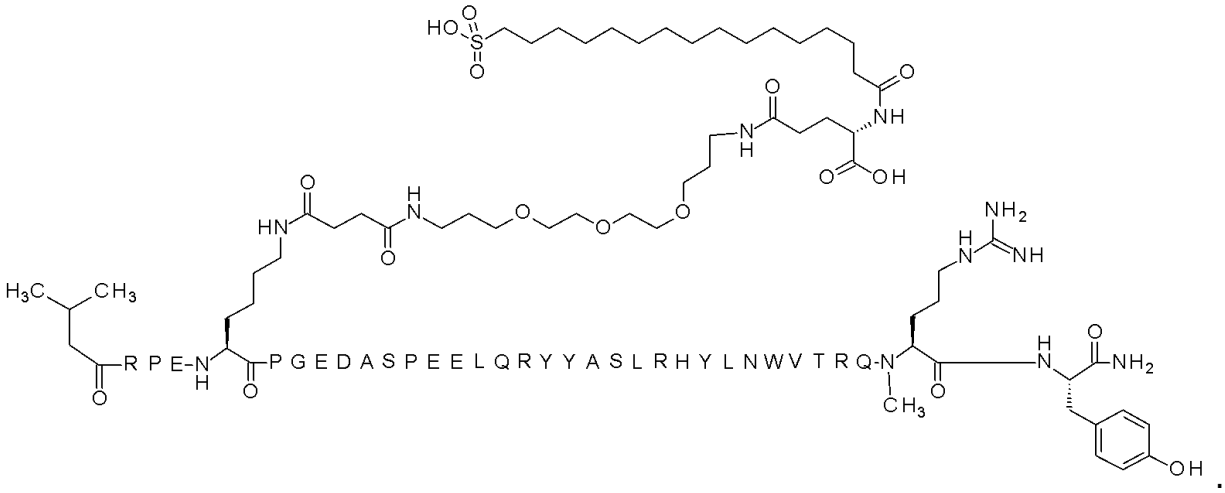


.

5. PYY-forbindelsen ifølge et hvilket som helst av kravene 1-3, hvori PYY-forbindelsen er
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[2-[2-[2-[[2-[2-[2-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)-butanoyl]amino]etoksy]etoksy]acetyl]amino]etoksy]-etoksy]acetyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO:18)



6. PYY-forbindelsen ifølge et hvilket som helst av kravene 1-3, hvori PYY-forbindelsen er
4-N{alfa}-(3-metylbutanoyl)-7-N{Epsilon}-[4-[3-[2-[2-[3-[[(4S)-4-karboksy-4-(16-sulfoheksadekanoylamino)butanoyl]amino]propoksy]etoksy]etoksy]propylamino]-4-oksobutanoyl]-[Arg4,Lys7,Gln18,Trp30,NMeArg35]hPYY(4-36) (SEQ ID NO: 27)



8. PYY-forbindelse ifølge et hvilket som helst av kravene 1-6, for anvendelse som et medikament.

9. PYY-forbindelse ifølge et hvilket som helst av kravene 1-6, for anvendelse ved behandling og/eller forebygging av alle former for diabetes og relaterte sykdommer, så som spiseforstyrrelser, diabeteskomplikasjoner, kardiovaskulære sykdommer og/eller søvnapné; og/eller for å forbedre lipidparametere, forbedre β-cellefunksjonen og/eller for å forsinke eller forebygge progresjon av diabetessykdom og/eller fedme.

10. Farmasøytisk sammensetning som omfatter en PYY-forbindelse ifølge et hvilket som helst av kravene 1-6, en GLP-1-agonist valgt fra liraglutid, semaglutid, eksenatid, dulaglutid, lixisenatid, taspoglutid og albiglutid og minst én farmasøytisk akseptabel eksipiens.

11. Farmasøytisk sammensetning ifølge krav 10, hvori GLP-1-agonisten er liraglutid eller semaglutid, og hvori PYY-forbindelsen er SEQ ID NO:18.

12. Farmasøytisk sammensetning ifølge et hvilket som helst av kravene 10-11, for anvendelse som et medikament.

13. Farmasøytisk sammensetning ifølge et hvilket som helst av kravene 10-11, for anvendelse ved behandling og/eller forebygging av alle former for diabetes og relaterte sykdommer, så som spiseforstyrrelser, diabeteskomplikasjoner, kardiovaskulære sykdommer og/eller søvnapné; og/eller for å forbedre lipidparametere, forbedre β-cellefunksjon og/eller for å forsinke eller forebygge progresjon av diabetessykdom og/eller spiseforstyrrelser, så som fedme.