Claims

1. A method for the cleavage of a solid phase-bound polypeptide from the solid phase, the method comprising contacting the solid phase, to which the polypeptide is bound, with a composition consisting essentially of trifluoroacetic acid and 1,2-ethanedithiol, at a temperature in the range of 23 °C to 29°C, wherein the composition is contacted for 3 to 5 h with the solid phase to which the polypeptide is bound, and wherein the solid phase comprises a Rink amide resin.

2. The method of claim 1, wherein the polypeptide is bound to the Rink amide resin by a linker.

3. The method of any one of the preceding claims, wherein the composition comprises trifluoroacetic acid in an amount of 95 to 99 % v/v, and 1,2-ethanedithiol in an amount of 1 to 5 % v/v.

4. The method of any one of the preceding claims, wherein the composition essentially consists of trifluoroacetic acid in an amount of 97 % v/v, and 1,2-ethanedithiol in an amount of 3 % v/v.

5. The method of any one of the preceding claims, wherein the composition is contacted with the solid phase to which the polypeptide is bound, at a temperature of 25°C to 27°C, preferably at a temperature of 26°C.

6. The method of any one of the preceding claims, wherein the polypeptide is a GLP-1 agonist selected from GLP-1, exendin-3, liraglutide, albiglutide, dulaglutide, semaglutide, exendin-4 and analogues of exendin-4 selected from the group consisting of:
H-desPro^{36}-exendin-4-Lys$_6$-NH$_2$,
H-des(Pro^{36,37})-exendin-4-Lys$_4$-NH$_2$,
H-des(Pro^{36,37})-exendin-4-Lys$_5$-NH$_2$,
desPro^{36}[Asp^{28}]exendin-4 (1-39),
desPro^{36}[IsoAsp^{28}]exendin-4 (1-39),
desPro^{36}[Met(O)^{14},Asp^{28}]exendin-4 (1-39),

desPro^{36}[Met(O)^{14},IsoAsp^{28}]exendin-4 (1-39),
desPro^{36}[Trp(O$_2$)^{25},Asp^{28}]exendin-4 (1-39),
desPro^{36}[Trp(O$_2$)^{25},IsoAsp^{28}]exendin-4 (1-39),
desPro^{36}[Met(O)$_{14}$Trp(O$_2$)^{25},Asp^{28}]exendin-4 (1-39),
desPro^{36}[Met(O)$_{14}$Trp(O2)^{25},IsoAsp^{28}]exendin-4(1-39)
desPro^{36}[Asp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[IsoAsp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Met(O)^{14},Asp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Met(O)^{14},IsoAsp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Trp(O$_2$)^{25},Asp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Trp(O$_2$)^{25},IsoAsp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Met(O)^{14}Trp(O$_2$)^{25},Asp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Met(O)^{14}Trp(O$_2$)^{25},IsoAsp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36}[Asp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
desAsp^{28}Pro^{36},Pro^{37},Pro^{38}exendin-4(1-39)-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-NH$_2$,
desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
H-desAsp^{28} Pro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25}]exendin-4(1-39)-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-NH$_2$,
desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
desMet(O)^{14} Asp^{28} Pro^{36}, Pro^{37}, Pro^{38}exendin-4(1-39)-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}] exendin-4(1-39)-NH$_2$,
desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,

H-$(Lys)_6$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-Lys_6-NH_2,
H-Asn-$(Glu)_5$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}] exendin-4(1-39)-$(Lys)_6$-NH_2,
H-$(Lys)_6$-desPro^{36}[Met(O)^{14}, Trp$(O_2)^{25}$,Asp^{28}]exendin-4(1-39)-Lys_6-NH_2,
desAsp^{28}Pro^{36},Pro^{37},Pro^{38}[Met(O)^{14}, Trp$(O_2)^{25}$]exendin-4(1-39)-NH_2,
H-$(Lys)_6$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14}, Trp$(O_2)^{25}$,Asp^{28}]exendin-4(1-39)-NH_2,
H-Asn-$(Glu)_5$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-NH_2,
desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14}, Trp$(O_2)^{25}$,Asp^{28}]exendin-4(1-39)-$(Lys)_6$-NH_2,
H-$(Lys)_6$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Trp$(O_2)^{25}$,Asp^{28}]exendin-4(1-39)-$(Lys)_6$-NH_2,
H-Asn-$(Glu)_5$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Trp$(O_2)^{25}$,Asp^{28}]exendin-4(1-39)-$(Lys)_6$-NH_2,
and pharmaceutically acceptable salts thereof.

7. The method of claim 6, wherein the polypeptide is selected from exendin-4, lixisenatide, albiglutide, dulaglutide and semaglutide.

8. A method for the solid-phase synthesis of a polypeptide comprising a pre-determined amino acid sequence, said method comprising*:*
   (a) coupling an amino acid building block, comprising an unprotected C-terminal carboxyl group and a protected N-terminal amino group, C-terminally to a solid phase comprising a Rink amide resin,
   (b) de-protecting the N-terminal amino group of the amino acid building block,
   (c) coupling an amino acid building block, comprising an unprotected C-terminal carboxyl group and a protected N-terminal amino group, C-terminally to the unprotected N-terminal amino of step (b),
   (d) optionally repeating steps (b) and (c), and
   (e) cleaving the polypeptide from the solid phase by the method of any one of the claims 1 to 7.

9. The method of claim 8, wherein the polypeptide is a GLP-1 agonist selected from GLP-1, exendin-3, liraglutide, albiglutide, dulaglutide, semaglutide, exendin-4 and analogues of exendin-4 selected from the group consisting of:
H-desPro^{36}-exendin-4-Lys$_6$-NH$_2$,
H-des(Pro^{36,37})-exendin-4-Lys$_4$-NH$_2$,
H-des(Pro^{36,37})-exendin-4-Lys$_5$-NH$_2$,
desPro^{36}[Asp^{28}]exendin-4 (1-39),
desPro^{36}[IsoAsp^{28}]exendin-4 (1-39),
desPro^{36}[Met(O)^{14},Asp^{28}]exendin-4 (1-39),
desPro^{36}[Met(O)^{14},IsoAsp^{28}]exendin-4 (1-39),
desPro^{36}[Trp(O$_2$)^{25},Asp^{28}]exendin-4 (1-39),
desPro^{36}[Trp(O$_2$)^{25},IsoAsp^{28}]exendin-4 (1-39),
desPro^{36}[Met(O)$_{14}$Trp(O$_2$)^{25},Asp^{28}]exendin-4 (1-39),
desPro^{36}[Met(O)$_{14}$Trp(O2)^{25},IsoAsp^{28}]exendin-4(1-39)
desPro^{36}[Asp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[IsoAsp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Met(O)^{14},Asp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Met(O)^{14},IsoAsp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Trp(O$_2$)^{25},Asp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Trp(O$_2$)^{25},IsoAsp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Met(O)^{14}Trp(O$_2$)^{25},Asp^{28}]exendin-4 (1-39)-Lys$_6$-NH$_2$,
desPro^{36}[Met(O)^{14}Trp(O$_2$)^{25},IsoAsp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36}[Asp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
desAsp^{28}Pro^{36},Pro^{37},Pro^{38}exendin-4(1-39)-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-NH$_2$,
desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
H-desAsp^{28} Pro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25}]exendin-4(1-39)-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-NH$_2$,

desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
desMet(O)^{14} Asp^{28} Pro^{36}, Pro^{37}, Pro^{38}exendin-4(1-39)-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}] exendin-4(1-39)-NH$_2$,
desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}] exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36}[Met(O)^{14}, Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-Lys$_6$-NH$_2$,
desAsp^{28}Pro^{36},Pro^{37},Pro^{38}[Met(O)^{14}, Trp(O$_2$)^{25}]exendin-4(1-39)-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14}, Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Asp^{28}]exendin-4(1-39)-NH$_2$,
desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14}, Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-(Lys)$_6$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
H-Asn-(Glu)$_5$-desPro^{36},Pro^{37},Pro^{38}[Met(O)^{14},Trp(O$_2$)^{25},Asp^{28}]exendin-4(1-39)-(Lys)$_6$-NH$_2$,
and pharmaceutically acceptable salts thereof.

10. The method of claim 8 or 9, wherein the polypeptide is selected from exendin-4, lixisenatide, albiglutide, dulaglutide and semaglutide.

11. Use of the composition consisting essentially of trifluoroacetic acid and 1,2-ethanedithiol, wherein the composition comprises trifluoroacetic acid in an amount of 97% to 99% v/v, and 1,2-ethanedithiol in an amount of 1% to 3% v/v, or the composition comprises trifluoroacetic acid in an amount of 97% v/v and 1,2-ethanedithiol in an amount of 3% v/v, in a solid phase synthesis

of a polypeptide, wherein the composition is in particular used to cleave the polypeptide from the solid phase.