CLAIMS

1. A fusion or conjugate composition comprising or consisting of (a) an insulinotropic agent or an incretin drug present as a fusion or a conjugate with, (b) a dAb which binds serum albumin selected from: (i) the DOM 7h-14 domain antibody (dAb) (the amino acid sequence of DOM 7h-14 is shown in Figure 1(h): SEQ ID NO 8), (ii) the DOM 7h-14-10 domain antibody (dAb) (the amino acid sequence of DOM 7h-14-10 is shown in Figure 1(o):SEQ ID NO 26) or a dAb which has up to 4 amino acid differences from the sequence of the DOM 7h-14-10 dAb; and (iii) the DOM 7h-11-15 dAb (the amino acid sequence of DOM 7h-11-15 is shown in Figure 1(p): SEQ ID NO 27) or (iv) the DOM 7h-14-10 R108C domain antibody (dAb) (the amino acid sequence of DOM 7h-14-10 is shown in Figure 1(r).

2. A fusion or conjugate according to claim 1, wherein the drug is an exendin-4, a GLP-1 molecule, or a PYY molecule, or a mutant or derivative thereof which retains binding activity of the native molecule.

3. A fusion or conjugate according to claim 1 or 2, wherein the drug is selected from (a) the GLP-1 (7-37) A8G mutant which has the amino acid sequence shown in figure 1 (i) (SEQ ID NO 9), or (b) the exendin-4 molecule which has the amino acid sequence shown in figure 1 (j) (SEQ ID NO 10) or (c) PYY3-36 or PYY 3-36 which has lysine at position 10 and has the amino acid sequence shown in Figure 1s.

4. A fusion or conjugate according to any of the preceding claims, which comprises an amino acid or chemical linker joining the drug and the dAb.

5. A fusion or conjugate according to claim 4, wherein the amino acid linker is a helical linker with the amino acid sequence shown in figure 1 (k) (SEQ ID NO 11), or the gly-ser linker with the amino acid sequence shown in figure 1 (l) (SEQ ID NO 12).

6. A fusion according to any of the preceding claims, wherein the insulinotropic agent or the incretin drug is present as part of a fusion at either the N-terminal or C-terminal of the dAb.

7. A fusion or conjugate according to claim 6, which comprises or consists of an amino acid sequence selected from the following:

(a) Exendin 4, (G4S)3, linker DOM7h-14-10 fusion **(DMS7139)**

HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGG
GGSDIQMTQSPSSLSASVGDRVTITCRASQWIGSQLSWYQQKPGKAPKLLIM
WRSSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQGLRHPKTFGQGT
KVEIKR
(SEQ ID NO 24)

(b) Exendin 4, (G4S)3, linker DOM7h-11-15 fusion **(DMS7143)**

HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGG
GGSDIQMTQSPSSLSASVGDRVTITCRASRPIGTMLSWYQQKPGKAPKLLILA
FSRLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQAGTHPTTFGQGTKV
EIKR
(SEQ ID NO 25)

(c) A peptide conjugate which is:
a DOM 7h-14-10 (R108C) AlbudAb conjugated to a C-terminally amidated PYY3-36 via a lysine (introduced at position 10 of PYY) and a 4 repeat PEG linker as shown in Figure 14.

8. A fusion or conjugate according to any of the preceding claims, wherein the dAb is further formatted to increase its hydrodynamic size by attaching molecules(s) to the dAb selected from the following: a PEG group, serum albumin, transferrin, transferrin receptor or at least the transferrin-binding portion thereof, an antibody Fc region, or by conjugation to an antibody domain.

9. A fusion or conjugate according to any of the preceding claims, which comprises additional dAb moieties which have the same or different binding specificities to the DOM 7h-14-10 or DOM 7h-11-15 dAbs.

10. A fusion or conjugate according to any of the preceding claims which has an elimination half life in a human of 12 hours or more e.g. 12-21 days.

11. A fusion or conjugate according to any of the preceding claims which binds to human serum albumin with KD in the range of about 5 micromolar to about 1 picomolar.

12. A pharmaceutical composition comprising a fusion or conjugate according to any of the preceding claims in combination with a pharmaceutically or physiologically acceptable carrier, excipient or diluent.

13. A composition which comprises (a) a fusion or conjugate according to any of claims 1-12 and (b) further therapeutic or active agents, for separate, sequential or concurrent administration to a subject.

14. A composition according to any of the preceding claims, for use in treating or preventing a metabolic disease or disorder .

15. A composition according to claim 14, wherein the disease or disorder is selected from: hyperglycemia , impaired glucose tolerance, beta cell deficiency, diabetes (type 1 or type 2 diabetes or gestational diabetes), obesity, or diseases characterised by by overeating.

CLAIMS

1. A drug fusion or conjugate comprising (a) an insulinotropic agent or an incretin drug selected from: (i) GLP-1, (ii) exendin-4, and (iii) PYY (Peptide YY), present as a fusion or a conjugate with (b) a dAb which binds serum albumin selected from: (i) the DOM 7h-14-10 domain antibody (dAb) (SEQ ID NO 26); (ii) the DOM 7h-11-15 dAb (SEQ ID NO 27); or (iii) the DOM 7h-14-10 R108C domain antibody (dAb) (SEQ ID NO 42).

2. The fusion or conjugate according to claim 1, wherein the drug is selected from (a) the GLP-1 (7-37) A8G mutant which has the amino acid sequence shown in figure 1 (i) (SEQ ID NO 9), or (b) the exendin-4 molecule which has the amino acid sequence shown in figure 1 (j) (SEQ ID NO 10) or (c) PYY3-36 or PYY 3-36 which has lysine at position 10 and has the amino acid sequence shown in Figure 1(s) (SEQ ID NO 43).

3. The fusion or conjugate according to claim 1, which comprises an amino acid or chemical linker joining the drug and the dAb.

4. The fusion or conjugate according to claim 3, wherein the amino acid linker is a helical linker with the amino acid sequence shown in figure 1 (k) (SEQ ID NO 11), or the gly-ser linker with the amino acid sequence shown in figure 1 (l) (SEQ ID NO 12).

5. The fusion or conjugate according to claim 1, wherein the insulinotropic agent or the incretin drug is present as part of a fusion at either the N-terminal or C-terminal of the dAb.

6. The fusion or conjugate according to claim 1, which comprises an amino acid sequence selected from the following:
(a) Exendin 4, (G4S)3, linker DOM7h-14-10 fusion (DMS7139)

HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGGGGSD
IQMTQSPSSLSASVGDRVTITCRASQWIGSQLSWYQQKPGKAPKLLIMWRSSLQSGVP
SRFSGSGSGTDFTLTISSLQPEDFATYYCAQGLRHPKTFGQGTKVEIKR (SEQ ID NO
24),

(b) Exendin 4, (G4S)3, linker DOM7h-11-15 fusion (DMS7143)

HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGGGGSD IQMTQSPSSLSASVGDRVTITCRASRPIGTMLSWYQQKPGKAPKLLILAFSRLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCAQAGTHPTTFGQGTKVEIKR (SEQ ID NO 25), or

(c) A peptide conjugate which is:

a DOM 7h-14-10 (R108C) AlbudAb conjugated to a C-terminally amidated PYY3-36 via a lysine (introduced at position 10 of PYY) and a 4 repeat PEG linker as shown in Figure 14.

7. The fusion or conjugate according to claim 1, wherein the dAb is further formatted to increase its hydrodynamic size by attaching molecule(s) to the dAb selected from the following: a PEG group, serum albumin, transferrin, transferrin receptor or at least the transferrin-binding portion thereof, an antibody Fc region, or by conjugation to an antibody domain.

8. The fusion or conjugate according to claim 1, which comprises additional dAb moieties which have the same or different binding specificities to the DOM 7h-14-10 or DOM 7h-11-15 dAbs.

9. The fusion or conjugate according to claim 1, which has an elimination half life in a human of 12 hours or 12-21 days.

10. The fusion or conjugate according to claim 1, which binds to human serum albumin with KD in the range of about 5 micromolar to about 1 picomolar.

11. A pharmaceutical composition comprising the fusion or conjugate according to claim 1, in combination with a pharmaceutically or physiologically acceptable carrier, excipient or diluent.

12. The composition according to claim 11 further comprises therapeutic or active agents, for separate, sequential or concurrent administration to a subject.

13. The composition according to claim 11, for use in treating a metabolic disease or disorder wherein the metabolic disease or disorder is selected from the group consisting of hyperglycemia, impaired glucose tolerance, beta cell deficiency, diabetes (type 1 or type 2 diabetes or gestational diabetes), obesity, and diseases characterized by overeating.