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(57) **Abrégé/Abstract:**

The invention relates to improved variants of the anti-serum albumin immunoglobulin single variable domain DOM7h-14, as well as ligands and drug conjugates comprising such variants, compositions, nucleic acids, vectors and hosts.

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IMPROVED ANTI-SERUM ALBUMIN BINDING VARIANTS

The invention relates to improved variants of the anti-serum albumin immunoglobulin single variable domain DOM7h-14, as well as ligands and drug
5 conjugates comprising such variants, compositions, nucleic acids, vectors and hosts.

BACKGROUND OF THE INVENTION

WO04003019 and WO2008/096158 disclose anti-serum albumin (SA) binding moieties, such as anti-SA immunoglobulin single variable domains (dAbs), which have
10 therapeutically-useful half-lives. These documents disclose monomer anti-SA dAbs as well as multi-specific ligands comprising such dAbs, eg, ligands comprising an anti-SA dAb and a dAb that specifically binds a target antigen, such as TNFR1. Binding moieties are disclosed that specifically bind serum albumins from more than one species, eg human/mouse cross-reactive anti-SA dAbs.

15 WO05118642 and WO2006/059106 disclose the concept of conjugating or associating an anti-SA binding moiety, such as an anti-SA immunoglobulin single variable domain, to a drug, in order to increase the half-life of the drug. Protein, peptide and NCE (new chemical entity) drugs are disclosed and exemplified. WO2006/059106 discloses the use of this concept to increase the half-life of insulintropic agents, eg,
20 incretin hormones such as glucagon-like peptide (GLP)-1.

Reference is also made to Holt *et al*, "Anti-Serum albumin domain antibodies for extending the half-lives of short lived drugs", Protein Engineering, Design & Selection, vol 21, no 5, pp283-288, 2008.

WO2008/096158 discloses DOM7h-14, which is a good anti-SA dAb. It would
25 be desirable to provide improved dAbs that are variants of DOM7h-14 and that specifically bind serum albumin, preferably albumins from human and non-human species, which would provide utility in animal models of disease as well as for human therapy and/or diagnosis. It would also be desirable to provide for the choice between

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relatively modest- and high-affinity anti-SA binding moieties (dAbs). Such moieties could be linked to drugs, the anti-SA binding moiety being chosen according to the contemplated end-application. This would allow the drug to be better tailored to treating and/or preventing chronic or acute indications, depending upon the choice of anti-SA binding moiety. It would also be desirable to provide anti-dAbs, that are monomeric or substantially so in solution. This would especially be advantageous when the anti-SA dAb is linked to a binding moiety, eg, a dAb, that specifically binds a cell-surface receptor, such as TNFR1, with the aim of antagonizing the receptor. The monomeric state of the anti-SA dAb is useful in reducing the chance of receptor cross-linking, since multimers are less likely to form which could bind and cross-link receptors (eg, TNFR1) on the cell surface, thus increasing the likelihood of receptor agonism and detrimental receptor signaling.

SUMMARY OF THE INVENTION

Aspects of the present invention solve these problems.

To this end, the present inventors surprisingly found that beneficial mutations can be targeted to the CDR3 region 92 to 96 (position numbering according to Kabat) compared of DOM7h-14.

In one aspect the invention, therefore, provides an anti-serum albumin (SA) immunoglobulin single variable domain variant of DOM7h-14, wherein the variant comprises at least one mutation in CDR3 region 92 to 96 (position numbering according to Kabat) compared to DOM7h-14, and wherein the variant has from 1 to 8 changes compared to the amino acid sequence of DOM7h-14. There is also provided an anti-serum albumin (SA) binding moiety comprising CDR3 of a variant of this aspect of the invention.

Another aspect of the invention provides an anti-serum albumin (SA) immunoglobulin single variable domain variant of DOM7h-14, wherein the variant comprises a Ser at position 22 and a Glu at position 42 (numbering according to Kabat)

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compared to DOM7h-14, and wherein the variant has from 0 to 4 further changes compared to the amino acid sequence of DOM7h-14.

Embodiments of any aspect of the invention provide DOM7h-14 variants of good anti-serum albumin affinities. The choice of variant can allow for tailoring of half-life according to the desired therapeutic and/or prophylactic setting. For example, in one embodiment, the affinity of the variant for serum albumin is relatively high, such that the variant would be useful for inclusion in products that find utility in treating and/or preventing chronic or persistent diseases, conditions, toxicity or other chronic indications. In one embodiment, the affinity of the variant for serum albumin is relatively modest, such that the variant would be useful for inclusion in products that find utility in treating and/or preventing acute diseases, conditions, toxicity or other acute indications. In one embodiment, the affinity of the variant for serum albumin is intermediate, such that the variant would be useful for inclusion in products that find utility in treating and/or preventing acute or chronic diseases, conditions, toxicity or other acute or chronic indications.

It is conceivable that a molecule with an appropriately high affinity and specificity for serum albumin would stay in circulation long enough to have the desired therapeutic effect. (Tomlinson, *Nature Biotechnology* **22**, 521 - 522 (2004)). Here, a high affinity anti-SA variant would stay in serum circulation matching that of the species' serum albumin (WO2008096158). Once in circulation, any fused therapeutic agent to the AlbuAb™ variant (an AlbuAb is an anti-serum albumin dAb or immunoglobulin single variable domain), be it NCE, peptide or protein, consequently would be able to act longer on its target and exhibit a longer lasting therapeutic effect. This would allow for targeting chronic or persistent diseases without the need of frequent dosing.

A variant with moderate affinity (but specificity to SA) would only stay in serum circulation for a short time (eg, for a few hours or a few days) allowing for the specific targeting of therapeutic targets involved in acute diseases by the fused therapeutic agent.

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This way it is possible to tailor the anti-SA-containing product to the therapeutic disease area by choosing an anti-SA variant with the appropriate albumin binding affinity and/or serum half-life.

5 An aspect of the invention provides a multispecific ligand comprising any anti-SA variant as described above and a binding moiety that specifically binds a target antigen other than SA.

10 An aspect of the invention provides a fusion product, eg, a fusion protein or fusion with a peptide or NCE (new chemical entity) drug, comprising a polypeptide, protein, peptide or NCE drug fused or conjugated (for an NCE) to any variant as described above, wherein the variant is DOM7h-14-10 (or a variant having an amino acid that is at least 95, 96, 97, 98 or 99% identical to the amino acid sequence of DOM7h-14-10). DOM7h-14-10 gives only a modest drop in affinity when fused or conjugated to partner, making it useful in fusion products.

15 An aspect of the invention provides a composition comprising a variant, fusion protein or ligand of any preceding aspect and a pharmaceutically acceptable diluent, carrier, excipient or vehicle.

An aspect of the invention provides a method of treating or preventing a disease or disorder in a patient, comprising administering at least one dose of a variant according to any aspect or embodiment of the invention to said patient.

20 An aspect of the invention provides a polypeptide fusion or conjugate comprising an anti-serum albumin dAb as disclosed herein (eg, DOM7h-14-10) and an incretin or insulintropic agent, eg, exendin-4, GLP-1(7-37), GLP-1(6-36) or any incretin or insulintropic agent disclosed in WO06/059106, these agents being explicitly incorporated herein by reference as though written herein for inclusion in the
25 present invention and claims below.

BRIEF DESCRIPTION OF THE DRAWINGS

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Figure 1: Amino-acid sequence alignment for DOM7h-14 variant dAbs. A “.” at a particular position indicates the same amino as found in DOM7h-14 at that position. The CDRs are indicated by underlining and bold text (the first underlined sequence is CDR1, the second underlined sequence is CDR2 and the third underlined sequence is CDR3).

Figure 2: Kinetic parameters of DOM7h-14 variants. KD units = nM; Kd units = sec^{-1} ; Ka units = $\text{M}^{-1} \text{sec}^{-1}$. The notation A e-B means $A \times 10^{-B}$ and C e D means $C \times 10^D$.

The overall kinetic ranges in various species, as supported by the examples below, are indicated. Optional ranges are also provided for use in particular therapeutic settings (acute or chronic indications, conditions or diseases and “intermediate” for use in both chronic and acute settings). High affinity dAbs and products comprising these are useful for chronic settings. Medium affinity dAbs and products comprising these are useful for intermediate settings. Low affinity dAbs and products comprising these are useful for acute settings. The affinity in this respect is the affinity for serum albumin.

Various example anti-serum dAbs and fusion proteins are listed, and these support the ranges disclosed. Many of the examples have favourable kinetics in human and one or more non-human animals (eg, in human and *Cynomolgus* monkey and/or mouse). Choice of dAb or product comprising this can be tailored, according to the invention, depending on the setting (eg, chronic or acute) to be treated therapeutically.

DETAILED DESCRIPTION OF THE INVENTION

Within this specification the invention has been described, with reference to embodiments, in a way which enables a clear and concise specification to be written. It is intended and should be appreciated that embodiments may be variously combined or separated without parting from the invention.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art (e.g., in cell culture, molecular genetics, nucleic acid chemistry, hybridization techniques and

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biochemistry). Standard techniques are used for molecular, genetic and biochemical methods (see generally, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2d ed. (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. and Ausubel *et al.*, Short Protocols in Molecular Biology (1999) 4th Ed, John Wiley & Sons, Inc.) and chemical methods.

As used herein, the term “antagonist of Tumor Necrosis Factor Receptor 1 (TNFR1)” or “anti-TNFR1 antagonist” or the like refers to an agent (e.g., a molecule, a compound) which binds TNFR1 and can inhibit a (i.e., one or more) function of TNFR1. For example, an antagonist of TNFR1 can inhibit the binding of TNF α to TNFR1 and/or inhibit signal transduction mediated through TNFR1. Accordingly, TNFR1-mediated processes and cellular responses (e.g., TNF α -induced cell death in a standard L929 cytotoxicity assay) can be inhibited with an antagonist of TNFR1.

A “patient” is any animal, eg, a mammal, eg, a non-human primate (such as a baboon, rhesus monkey or Cynomolgus monkey), mouse, human, rabbit, rat, dog, cat or pig. In one embodiment, the patient is a human.

As used herein, “peptide” refers to about two to about 50 amino acids that are joined together via peptide bonds.

As used herein, “polypeptide” refers to at least about 50 amino acids that are joined together by peptide bonds. Polypeptides generally comprise tertiary structure and fold into functional domains.

As used herein an antibody refers to IgG, IgM, IgA, IgD or IgE or a fragment (such as a Fab, F(ab')₂, Fv, disulphide linked Fv, scFv, closed conformation multispecific antibody, disulphide-linked scFv, diabody) whether derived from any species naturally producing an antibody, or created by recombinant DNA technology; whether isolated from serum, B-cells, hybridomas, transfectomas, yeast or bacteria.

As used herein, “antibody format” refers to any suitable polypeptide structure in which one or more antibody variable domains can be incorporated so as to confer binding specificity for antigen on the structure. A variety of suitable antibody formats are known in the art, such as, chimeric antibodies, humanized antibodies, human antibodies, single chain antibodies, bispecific antibodies, antibody heavy chains,

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antibody light chains, homodimers and heterodimers of antibody heavy chains and/or light chains, antigen-binding fragments of any of the foregoing (*e.g.*, a Fv fragment (*e.g.*, single chain Fv (scFv), a disulfide bonded Fv), a Fab fragment, a Fab' fragment, a F(ab')₂ fragment), a single antibody variable domain (*e.g.*, a dAb, V_H, V_{HH}, V_L), and
 5 modified versions of any of the foregoing (*e.g.*, modified by the covalent attachment of polyethylene glycol or other suitable polymer or a humanized V_{HH}).

The phrase "immunoglobulin single variable domain" refers to an antibody variable domain (V_H, V_{HH}, V_L) that specifically binds an antigen or epitope independently of different V regions or domains. An immunoglobulin single variable
 10 domain can be present in a format (*e.g.*, homo- or hetero-multimer) with other variable regions or variable domains where the other regions or domains are not required for antigen binding by the single immunoglobulin variable domain (*i.e.*, where the immunoglobulin single variable domain binds antigen independently of the additional variable domains). A "domain antibody" or "dAb" is the same as an "immunoglobulin
 15 single variable domain" as the term is used herein. A "single immunoglobulin variable domain" is the same as an "immunoglobulin single variable domain" as the term is used herein. A "single antibody variable domain" or an "antibody single variable domain" is the same as an "immunoglobulin single variable domain" as the term is used herein. An immunoglobulin single variable domain is in one embodiment a human antibody
 20 variable domain, but also includes single antibody variable domains from other species such as rodent (for example, as disclosed in WO 00/29004), nurse shark and *Camelid* V_{HH} dAbs.

Camelid V_{HH} are immunoglobulin single variable domain polypeptides that are derived from species including camel, llama, alpaca, dromedary, and guanaco, which produce
 25 heavy chain antibodies naturally devoid of light chains. The V_{HH} may be humanized.

A "domain" is a folded protein structure which has tertiary structure independent of the rest of the protein. Generally, domains are responsible for discrete functional properties of proteins, and in many cases may be added, removed or transferred to other proteins without loss of function of the remainder of the protein
 30 and/or of the domain. A "single antibody variable domain" is a folded polypeptide

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domain comprising sequences characteristic of antibody variable domains. It therefore includes complete antibody variable domains and modified variable domains, for example, in which one or more loops have been replaced by sequences which are not characteristic of antibody variable domains, or antibody variable domains which have
5 been truncated or comprise N- or C-terminal extensions, as well as folded fragments of variable domains which retain at least the binding activity and specificity of the full-length domain.

In the instant application, the term “prevention” and “preventing” involves administration of the protective composition prior to the induction of the disease or
10 condition. “Treatment” and “treating” involves administration of the protective composition after disease or condition symptoms become manifest. “Suppression” or “suppressing” refers to administration of the composition after an inductive event, but prior to the clinical appearance of the disease or condition.

As used herein, the term “dose” refers to the quantity of ligand administered to a
15 subject all at one time (unit dose), or in two or more administrations over a defined time interval. For example, dose can refer to the quantity of ligand (*e.g.*, ligand comprising an immunoglobulin single variable domain that binds target antigen) administered to a subject over the course of one day (24 hours) (daily dose), two days, one week, two weeks, three weeks or one or more months (*e.g.*, by a single administration, or by two
20 or more administrations). The interval between doses can be any desired amount of time. The term “pharmaceutically effective” when referring to a dose means sufficient amount of the ligand, domain or pharmaceutically active agent to provide the desired effect. The amount that is “effective” will vary from subject to subject, depending on the age and general condition of the individual, the particular drug or pharmaceutically
25 active agent and the like. Thus, it is not always possible to specify an exact “effective” amount applicable for all patients. However, an appropriate “effective” dose in any individual case may be determined by one of ordinary skill in the art using routine experimentation.

Methods for pharmacokinetic analysis and determination of ligand (*eg*, single
30 variable domain, fusion protein or multi-specific ligand) half-life will be familiar to

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those skilled in the art. Details may be found in *Kenneth, A et al*: Chemical Stability of Pharmaceuticals: A Handbook for Pharmacists and in *Peters et al*, Pharmacokinetic analysis: A Practical Approach (1996). Reference is also made to “Pharmacokinetics”, M Gibaldi & D Perron, published by Marcel Dekker, 2nd Rev. ex edition (1982), which describes pharmacokinetic parameters such as t_{α} and t_{β} half lives and area under the curve (AUC). Optionally, all pharmacokinetic parameters and values quoted herein are to be read as being values in a human. Optionally, all pharmacokinetic parameters and values quoted herein are to be read as being values in a mouse or rat or *Cynomolgus* monkey.

Half lives ($t_{1/2\alpha}$ and $t_{1/2\beta}$) and AUC can be determined from a curve of serum concentration of ligand against time. The WinNonlin analysis package, eg version 5.1 (available from Pharsight Corp., Mountain View, CA94040, USA) can be used, for example, to model the curve. When two-compartment modeling is used, in a first phase (the alpha phase) the ligand is undergoing mainly distribution in the patient, with some elimination. A second phase (beta phase) is the phase when the ligand has been distributed and the serum concentration is decreasing as the ligand is cleared from the patient. The t_{α} half life is the half life of the first phase and the t_{β} half life is the half life of the second phase. Thus, in one embodiment, in the context of the present invention, the variable domain, fusion protein or ligand has a t_{α} half-life in the range of (or of about) 15 minutes or more. In one embodiment, the lower end of the range is (or is about) 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 10 hours, 11 hours or 12 hours. In addition, or alternatively, the variable domain, fusion protein or ligand according to the invention will have a t_{α} half life in the range of up to and including 12 hours (or about 12 hours). In one embodiment, the upper end of the range is (or is about) 11, 10, 9, 8, 7, 6 or 5 hours. An example of a suitable range is (or is about) 1 to 6 hours, 2 to 5 hours or 3 to 4 hours.

In one embodiment, the present invention provides the variable domain, fusion protein or ligand according to the invention has a t_{β} half-life in the range of (or of about) 2.5 hours or more. In one embodiment, the lower end of the range is (or is about) 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 10 hours, 11 hours, or 12 hours. In

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addition, or alternatively, the t_{β} half-life is (or is about) up to and including 21 or 25 days. In one embodiment, the upper end of the range is (or is about) 12 hours, 24 hours, 2 days, 3 days, 5 days, 10 days, 15 days, 19 days, 20 days, 21 days or 22 days. For example, the variable domain, fusion protein or ligand according to the invention will
5 have a t_{β} half life in the range 12 to 60 hours (or about 12 to 60 hours). In a further embodiment, it will be in the range 12 to 48 hours (or about 12 to 48 hours). In a further embodiment still, it will be in the range 12 to 26 hours (or about 12 to 26 hours).

As an alternative to using two-compartment modeling, the skilled person will be familiar with the use of non-compartmental modeling, which can be used to determine
10 terminal half-lives (in this respect, the term "terminal half-life" as used herein means a terminal half-life determined using non-compartmental modeling). The WinNonlin analysis package, eg version 5.1 (available from Pharsight Corp., Mountain View, CA94040, USA) can be used, for example, to model the curve in this way. In this instance, in one embodiment the single variable domain, fusion protein or ligand has a
15 terminal half life of at least (or at least about) 8 hours, 10 hours, 12 hours, 15 hours, 28 hours, 20 hours, 1 day, 2 days, 3 days, 7 days, 14 days, 15 days, 16 days, 17 days, 18 days, 19 days, 20 days, 21 days, 22 days, 23 days, 24 days or 25 days. In one embodiment, the upper end of this range is (or is about) 24 hours, 48 hours, 60 hours or 72 hours or 120 hours. For example, the terminal half-life is (or is about) from 8 hours
20 to 60 hours, or 8 hours to 48 hours or 12 to 120 hours, eg, in man.

In addition, or alternatively to the above criteria, the variable domain, fusion protein or ligand according to the invention has an AUC value (area under the curve) in the range of (or of about) 1 mg.min/ml or more. In one embodiment, the lower end of the range is (or is about) 5, 10, 15, 20, 30, 100, 200 or 300 mg.min/ml. In addition, or
25 alternatively, the variable domain, fusion protein or ligand according to the invention has an AUC in the range of (or of about) up to 600 mg.min/ml. In one embodiment, the upper end of the range is (or is about) 500, 400, 300, 200, 150, 100, 75 or 50 mg.min/ml. Advantageously the variable domain, fusion protein or ligand will have an AUC in (or about in) the range selected from the group consisting of the following: 15
30 to 150 mg.min/ml, 15 to 100 mg.min/ml, 15 to 75 mg.min/ml, and 15 to 50mg.min/ml.

“Surface Plasmon Resonance”: Competition assays can be used to determine if a specific antigen or epitope, such as human serum albumin, competes with another antigen or epitope, such as cynomolgus serum albumin, for binding to a serum albumin binding ligand described herein, such as a specific dAb. Similarly competition assays
5 can be used to determine if a first ligand such as dAb, competes with a second ligand such as a dAb for binding to a target antigen or epitope. The term “competes” as used herein refers to substance, such as a molecule, compound, preferably a protein, which is able to interfere to any extent with the specific binding interaction between two or more molecules. The phrase “does not competitively inhibit” means that substance, such as a
10 molecule, compound, preferably a protein, does not interfere to any measurable or significant extent with the specific binding interaction between two or more molecules. The specific binding interaction between two or more molecules preferably includes the specific binding interaction between a single variable domain and its cognate partner or target. The interfering or competing molecule can be another single variable domain or
15 it can be a molecule that is structurally and/or functionally similar to a cognate partner or target.

The term “binding moiety” refers to a domain that specifically binds an antigen or epitope independently of a different epitope or antigen binding domain. A binding moiety may be a domain antibody (dAb) or may be a domain which is a derivative of a
20 non-immunoglobulin protein scaffold, eg, a scaffold selected from the group consisting of CTLA-4, lipocalin, SpA, an affibody, an avimer, GroEl, transferrin, GroES and fibronectin, which binds to a ligand other than the natural ligand (in the case of the present invention, the moiety binds serum albumin). See WO2008/096158, which discloses examples of protein scaffolds and methods for selecting antigen or epitope-
25 specific binding domains from repertoires (see Examples 17 to 25), the disclosures of WO2008/096158 useful for the present invention.

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In a first aspect, the invention provides an anti-serum albumin (SA) immunoglobulin single variable domain variant of DOM7h-14, wherein the variant comprises at least one mutation in CDR3 region 92 to 96 (position numbering according to Kabat) compared to DOM7h-14, and wherein the variant has from 1 to 8 changes
 5 compared to the amino acid sequence of DOM7h-14.

Optionally, the variant comprises a AQG(X1)(X2)(X3)P(X4)T motif, wherein A is at position 89 (according to Kabat), and at least one of (X1) to (X4) represents an amino acid change compared to the sequence of DOM7h-14.

In one embodiment, position 95 (according to Kabat) is Pro. Additionally or
 10 alternatively, in one embodiment position 89 (according to Kabat) is Ala. Additionally or alternatively, in one embodiment position 90 (according to Kabat) is Gln. Additionally or alternatively, in one embodiment position 91 (according to Kabat) is Gly. Additionally or alternatively, in one embodiment position 97 (according to Kabat) is Thr.

15 In an embodiment, the variant comprises a mutation at each of positions 92, 93 and 94 and optionally position 96 (numbering according to Kabat) compared to DOM7h-14.

Optionally, the variant comprises one or more amino acid residues selected from

20 Position 92 = L or F,
 Position 93 = R, M or K,
 Position 94 = H or K, and

Position 96 = K or M (numbering according to Kabat).

25 In one embodiment, the variant comprises a Lys or Met at position 96 (numbering according to Kabat) compared to DOM7h-14. In this embodiment, optionally the variant comprises one or more amino acid residues selected from

Position 92 = L or F,

30 Position 93 = R, M or K, and

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Position 94 = H or K (numbering according to Kabat).

In one embodiment, the variant comprises an amino acid sequence that is identical to the amino acid sequence of a single variable domain selected from DOM7h-14-10, DOM7h-14-18, DOM7h-14-28 and DOM7h-14-36 or has up to 4 changes compared to the selected amino acid sequence, wherein the variant comprises at least one mutation in CDR3 region 92 to 96 (position numbering according to Kabat) compared to DOM7h-14.

An aspect of the invention provides an anti-serum albumin (SA) binding moiety comprising CDR3 of a variant according to the first aspect of the invention. In one embodiment, the SA-binding moiety comprises CDR1 of the selected variant or an amino acid sequence that is at least 50% identical to CDR1 of the selected variant. Additionally or alternatively, in an embodiment the SA-binding moiety comprises CDR2 of the selected variant or an amino acid sequence that is at least 50% identical to CDR2 of the selected variant.

In a further aspect of the invention, there is provided an anti-serum albumin (SA) immunoglobulin single variable domain variant of DOM7h-14, wherein the variant comprises a Ser at position 22 and a Glu at position 42 (numbering according to Kabat) compared to DOM7h-14, and wherein the variant has from 0 to 4 further changes compared to the amino acid sequence of DOM7h-14. In one embodiment, the variant comprises an amino acid sequence that is identical to the amino acid sequence of DOM7h-14-19 or has up to 4 changes compared to the amino acid sequence of DOM7h-14-19, wherein the variant comprises a Ser at position 22 and a Glu at position 42 (numbering according to Kabat) compared to DOM7h-14.

In one embodiment, the variant or binding moiety according to any aspect or embodiment of the invention comprises one or more of the following kinetic characteristics:-

- (a) The variant or moiety comprises a binding site that specifically binds human SA with a dissociation constant (KD) from (or from about) 0.1 to (or to about)

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10000 nM, optionally from (or from about) 1 to (or to about) 6000 nM, as determined by surface plasmon resonance;

- 5 (b) The variant or moiety comprises a binding site that specifically binds human SA with an off-rate constant (K_d) from (or from about) 1.5×10^{-4} to (or to about) 0.1 sec^{-1} , optionally from (or from about) 3×10^{-4} to (or to about) 0.1 sec^{-1} as determined by surface plasmon resonance;
- 10 (c) The variant or moiety comprises a binding site that specifically binds human SA with an on-rate constant (K_a) from (or from about) 2×10^6 to (or to about) $1 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$, optionally from (or from about) 1×10^6 to (or to about) $2 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$ as determined by surface plasmon resonance;
- (d) The variant or moiety comprises a binding site that specifically binds *Cynomolgus* monkey SA with a dissociation constant (KD) from (or from about) 0.1 to (or to about) 10000 nM, optionally from (or from about) 1 to (or to about) 6000 nM, as determined by surface plasmon resonance;
- 15 (e) The variant or moiety of any preceding claim, wherein the variant comprises a binding site that specifically binds *Cynomolgus* monkey SA with an off-rate constant (K_d) from (or from about) 1.5×10^{-4} to (or to about) 0.1 sec^{-1} , optionally from (or from about) 3×10^{-4} to (or to about) 0.1 sec^{-1} as determined by surface plasmon resonance;
- 20 (f) The variant or moiety of any preceding claim, wherein the variant comprises a binding site that specifically binds *Cynomolgus* monkey SA with an on-rate constant (K_a) from (or from about) 2×10^6 to (or to about) $1 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$, optionally from (or from about) 1×10^6 to (or to about) $5 \times 10^3 \text{ M}^{-1}\text{sec}^{-1}$ as determined by surface plasmon resonance;
- 25 (g) The variant or moiety comprises a binding site that specifically binds rat SA with a dissociation constant (KD) from (or from about) 1 to (or to about) 10000

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nM, optionally from (or from about) 20 to (or to about) 6000 nM, as determined by surface plasmon resonance;

(h) The variant or moiety comprises a binding site that specifically binds rat SA with an off-rate constant (K_d) from (or from about) 2×10^{-3} to (or to about) 0.15 sec^{-1} , optionally from (or from about) 9×10^{-3} to (or to about) 0.14 sec^{-1} as determined by surface plasmon resonance;

(i) The variant or moiety comprises a binding site that specifically binds rat SA with an on-rate constant (K_a) from (or from about) 2×10^6 to (or to about) $1 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$, optionally from (or from about) 1×10^6 to (or to about) $3 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$ as determined by surface plasmon resonance;

(j) The variant or moiety comprises a binding site that specifically binds mouse SA with a dissociation constant (K_D) from (or from about) 1 to (or to about) 10000 nM as determined by surface plasmon resonance;

(k) The variant or moiety comprises a binding site that specifically binds mouse SA with an off-rate constant (K_d) from (or from about) 2×10^{-3} to (or to about) 0.15 sec^{-1} as determined by surface plasmon resonance; and/or

(l) The variant or moiety comprises a binding site that specifically binds mouse SA with an on-rate constant (K_a) from (or from about) 2×10^6 to (or to about) $1 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$, optionally from (or from about) 2×10^6 to (or to about) $1.5 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$ as determined by surface plasmon resonance.

Optionally, the variant or moiety has

I: a K_D according to (a) and (d), a K_d according to (b) and (e), and a K_a according to (c) and (f); or

II: a K_D according to (a) and (g), a K_d according to (b) and (h), and a K_a according to (c) and (i); or

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III: a K_D according to (a) and (j), a K_d according to (b) and (k), and a K_a according to (c) and (l); or

IV: kinetics according to I and II; or

V: kinetics according to I and III; or

5 VI: kinetics according to I, II and III.

The invention also provides a ligand comprising a variant or moiety of any preceding aspect or embodiment of the invention. For example, the ligand can be a dual-specific ligand (see WO04003019 for examples of dual-specific ligands). In one aspect, the invention provides a multispecific ligand comprising an anti-SA variant or
 10 moiety of any preceding aspect or embodiment of the invention and a further binding moiety that specifically binds a target antigen other than SA. The or each binding moiety can be any binding moiety that specifically binds a target, eg, the moiety is an antibody, antibody fragment, scFv, Fab, dAb or a binding moiety comprising a non-immunoglobulin protein scaffold. Such moieties are disclosed in detail in
 15 WO2008/096158 (see examples 17 to 25).

Examples of non-immunoglobulin scaffolds are CTLA-4, lipocalin, staphylococcal protein A (spA), Affibody™, Avimers™, GroEL and fibronectin.

In one embodiment, a linker is provided between the anti-target binding moiety and the anti-SA single variant or moiety, the linker comprising the amino acid sequence
 20 AST, optionally ASTSGPS, eg, where anti-SA and anti-target dAbs are used. Alternative linkers are described in WO2007085814 and WO2008/096158 (see the passage at page 135, line 12 to page 140, line 14).

In one embodiment of the multispecific ligand, the target antigen may be, or be
 25 part of, polypeptides, proteins or nucleic acids, which may be naturally occurring or

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synthetic. In this respect, the ligand of the invention may bind the target antigen and act as an antagonist or agonist (e.g., EPO receptor agonist). One skilled in the art will appreciate that the choice is large and varied. They may be for instance, human or animal proteins, cytokines, cytokine receptors, where cytokine receptors include

5 receptors for cytokines, enzymes, co-factors for enzymes or DNA binding proteins. Suitable cytokines and growth factors include, but are preferably not limited to: ApoE, Apo-SAA, BDNF, Cardiotrophin-1, EGF, EGF receptor, ENA-78, Eotaxin, Eotaxin-2, Exodus-2, EpoR, FGF-acidic, FGF-basic, fibroblast growth factor-10, FLT3 ligand, Fractalkine (CX3C), GDNF, G-CSF, GM-CSF, GF- β 1, insulin, IFN- γ , IGF-I, IGF-II,

10 IL-1 α , IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8 (72 a.a.), IL-8 (77 a.a.), IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-16, IL-17, IL-18 (IGIF), Inhibin α , Inhibin β , IP-10, keratinocyte growth factor-2 (KGF-2), KGF, Leptin, LIF, Lymphotoxin, Mullerian inhibitory substance, monocyte colony inhibitory factor, monocyte attractant protein, M-CSF, MDC (67 a.a.), MDC (69 a.a.), MCP-1 (MCAF), MCP-2, MCP-3, MCP-4,

15 MDC (67 a.a.), MDC (69 a.a.), MIG, MIP-1 α , MIP-1 β , MIP-3 α , MIP-3 β , MIP-4, myeloid progenitor inhibitor factor-1 (MPIF-1), NAP-2, Neurturin, Nerve growth factor, β -NGF, NT-3, NT-4, Oncostatin M, PDGF-AA, PDGF-AB, PDGF-BB, PF-4, RANTES, SDF1 α , SDF1 β , SCF, SCGF, stem cell factor (SCF), TARC, TGF- α , TGF- β , TGF- β 2, TGF- β 3, tumour necrosis factor (TNF), TNF- α , TNF- β , TNF receptor I,

20 TNF receptor II, TNIL-1, TPO, VEGF, VEGF receptor 1, VEGF receptor 2, VEGF receptor 3, GCP-2, GRO/MGSA, GRO- β , GRO- γ , HCC1, 1-309, HER 1, HER 2, HER 3 and HER 4, CD4, human chemokine receptors CXCR4 or CCR5, non-structural protein type 3 (NS3) from the hepatitis C virus, , TNF-alpha, IgE, IFN-gamma, MMP-12, CEA, H. pylori, TB, influenza, Hepatitis E, MMP-12, internalizing receptors that

25 are over-expressed on certain cells, such as the epidermal growth factor receptor (EGFR), ErbB2 receptor on tumor cells, an internalising cellular receptor, LDL receptor, FGF2 receptor, ErbB2 receptor, transferrin receptor, PDGF receptor, VEGF receptor, PsmAr, an extracellular matrix protein, elastin, fibronectin, laminin, α 1-antitrypsin, tissue factor protease inhibitor, PDK1, GSK1, Bad, caspase-9, Forkhead, an

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antigen of *Helicobacter pylori*, an antigen of *Mycobacterium tuberculosis*, and an antigen of influenza virus. It will be appreciated that this list is by no means exhaustive.

In one embodiment, the multispecific ligand comprises an anti-SA dAb variant or moiety of the invention and an anti-TNFR1 binding moiety, eg, an anti-TNFR1 dAb.

5 Optionally, the ligand has only one anti-TNFR1 binding moiety (eg, dAb) to reduce the chance of receptor cross-linking. In one embodiment, the anti-SA dAb variant is DOM7h-14-10.

In one embodiment, the anti-TNFR1 binding moiety is DOM1h-131-206 disclosed in WO2008149148 (the amino acid sequence of which and the nucleotide
10 sequence of which, may be used with the present invention).

In one embodiment, the multispecific ligand comprises or consists of the amino acid sequence of DOM1h-131-206 and the amino acid sequence of DOM7h-14-10.

In one embodiment, the anti-TNFR1 binding moiety or dAb is any such moiety
15 or dAb disclosed in co-pending application USSN 61/153,746, the disclosure of which is incorporated herein by reference. In one embodiment, the anti-TNFR1 binding moiety comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of DOM1h-574-156, DOM1h-574-72, DOM1h-574-109, DOM1h-574-138, DOM1h-574-162 or DOM1h-574-180 or the amino acid sequence of any anti-
20 TNFR1 dAb disclosed in Table 3. In one embodiment, the multispecific ligand comprises or consists of the amino acid sequence of DOM1h-574-156 and the amino acid sequence of DOM7h-14-10.

In one embodiment, the ligand of the invention is a fusion protein comprising a variant or moiety of the invention fused directly or indirectly to one or more
25 polypeptides. For example, the fusion protein can be a "drug fusion" as disclosed in WO2005/118642, comprising a variant or moiety of the invention and a polypeptide drug as defined in that PCT application.

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As used herein, "drug" refers to any compound (e.g., small organic molecule, nucleic acid, polypeptide) that can be administered to an individual to produce a beneficial, therapeutic or diagnostic effect through binding to and/or altering the function of a biological target molecule in the individual. The target molecule can be an endogenous target molecule encoded by the individual's genome (e.g. an enzyme, receptor, growth factor, cytokine encoded by the individual's genome) or an exogenous target molecule encoded by the genome of a pathogen (e.g. an enzyme encoded by the genome of a virus, bacterium, fungus, nematode or other pathogen). Suitable drugs for use in fusion proteins and conjugates comprising an anti-SA dAb variant of the invention are disclosed in WO2005/118642 and WO2006/059106 (the entire list of specific drugs contemplated for inclusion with the present invention). For example, the drug can be glucagon-like peptide 1 (GLP-1) or a variant, interferon alpha 2b or a variant or exendin-4 or a variant.

In one embodiment, the invention provides a drug conjugate as defined and disclosed in WO2005/118642 and WO2006/059106, wherein the conjugate comprises a variant or moiety of the invention. In one example, the drug is covalently linked to the variant or moiety (eg, the variant or moiety and the drug are expressed as part of a single polypeptide). Alternatively, in an example, the drug is non-covalently bonded or associated with the variant or moiety. The drug can be covalently or noncovalently bonded to the variant or moiety directly or indirectly (e.g., through a suitable linker and/or noncovalent binding of complementary binding partners (e.g., biotin and avidin)). When complementary binding partners are employed, one of the binding partners can be covalently bonded to the drug directly or through a suitable linker moiety, and the complementary binding partner can be covalently bonded to the variant or moiety directly or through a suitable linker moiety. When the drug is a polypeptide or peptide, the drug composition can be a fusion protein, wherein the polypeptide or peptide, drug and the polypeptide binding moiety are discrete parts (moieties) of a continuous polypeptide chain. As described herein, the polypeptide binding moieties

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and polypeptide drug moieties can be directly bonded to each other through a peptide bond, or linked through a suitable amino acid, or peptide or polypeptide linker.

A ligand which contains one single variable domain (monomer) variant or moiety of the invention or more than one single variable domain or moiety (multimer, fusion protein, conjugate, and dual specific ligand as defined herein) which specifically binds to serum albumin, can further comprise one or more entities selected from, but preferably not limited to a label, a tag, an additional single variable domain, a dAb, an antibody, an antibody fragment, a marker and a drug. One or more of these entities can be located at either the COOH terminus or at the N terminus or at both the N terminus and the COOH terminus of the ligand comprising the single variable domain or moiety, (either immunoglobulin or non-immunoglobulin single variable domain). One or more of these entities can be located at either the COOH terminus, or the N terminus, or both the N terminus and the COOH terminus of the single variable domain or moiety which specifically binds serum albumin of the ligand which contains one single variable domain (monomer) or moiety or more than one single variable domains or moieties (multimer, fusion protein, conjugate, and dual specific ligand as defined herein). Non-limiting examples of tags which can be positioned at one or both of these termini include a HA, his or a myc tag. The entities, including one or more tags, labels and drugs, can be bound to the ligand which contains one single variable domain (monomer) or more than one single variable domain or moiety (multimer, fusion protein, conjugate, and dual specific ligand as defined herein), which binds serum albumin, either directly or through linkers as described above.

An aspect of the invention provides a fusion product, eg, a fusion protein or fusion with a peptide or conjugate with an NCE (new chemical entity) drug, comprising a polypeptide drug fused or conjugated (for an NCE) to any variant or moiety as described above, optionally wherein the variant or moiety is DOM7h-14-10 (or a variant having an amino acid that is at least 95, 96, 97, 98 or 99% identical to the amino acid sequence of DOM7h-14-10). DOM7h-14-10 gives only a modest drop in affinity when fused or conjugated to partner, making them useful in fusion products.

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The invention provides a composition comprising a variant, fusion protein, conjugate or ligand of any aspect of the invention and a pharmaceutically acceptable diluent, carrier, excipient or vehicle.

Also encompassed herein is an isolated nucleic acid encoding any of the

5 variants, moieties, fusion proteins, conjugates or ligands described herein, e.g., a ligand which contains one single variable domain (monomer) variant of the invention or more than one single variable domain (e.g., multimer, fusion protein, conjugate, and dual specific ligand as defined herein) variant which specifically binds to serum albumin, or which specifically binds both human serum albumin and at least one non-human serum

10 albumin, or functionally active fragments thereof. Also encompassed herein is a vector and/or an expression vector, a host cell comprising the vector, e.g., a plant or animal cell and/or cell line transformed with a vector, a method of expressing and/or producing one or more variants, moieties, fusion proteins or ligands which contains one single variable domain (monomer) variant or moiety or more than one single variable

15 domain variants or moieties (e.g., multimer, fusion protein, conjugate, and dual specific ligand as defined herein) which specifically binds to serum albumin, or fragment(s) thereof encoded by said vectors, including in some instances culturing the host cell so that the one or more variants, moieties, fusion proteins or ligands or fragments thereof are expressed and optionally recovering the ligand which contains one single variable

20 domain or moiety (monomer) or more than one single variable domain or moiety (e.g., multimer, fusion protein, conjugate, and dual specific ligand as defined herein) which specifically binds to serum albumin, from the host cell culture medium. Also encompassed are methods of contacting a ligand described herein with serum albumin, including serum albumin and/or non-human serum albumin(s), and/or one or more

25 targets other than serum albumin, where the targets include biologically active molecules, and include animal proteins, cytokines as listed above, and include methods where the contacting is *in vitro* as well as administering any of the variants, moieties, fusion proteins or ligands described herein to an individual host animal or cell *in vivo* and/or *ex vivo*. Preferably, administering ligands described herein which comprises a

30 single variable domain (immunoglobulin or non-immunoglobulin) directed to serum

albumin and/or non-human serum albumin(s), and one or more domains directed to one or more targets other than serum albumin, will increase the half life, including the T beta and/or terminal half life, of the anti-target ligand. Nucleic acid molecules encoding the variants, fusion proteins or single domain containing ligands or fragments thereof, including functional fragments thereof, are contemplated herein. Vectors encoding the nucleic acid molecules, including but preferably not limited to expression vectors, are contemplated herein, as are host cells from a cell line or organism containing one or more of these expression vectors. Also contemplated are methods of producing any variant, fusion protein or ligand, including, but preferably not limited to any of the aforementioned nucleic acids, vectors and host cells.

An aspect of the invention provides a nucleic acid comprising a nucleotide sequence encoding a variant according to the invention or a multispecific ligand of the invention or fusion protein of the invention.

An aspect of the invention provides a nucleic acid comprising the nucleotide sequence of a DOM7h-14 variant selected from DOM7h-14-10, DOM7h-14-18, DOM7h-14-28, DOM7h-14-36 and DOM7h-14-19 or a nucleotide sequence that is at least 70, 75, 80, 85, 90, 95, 96, 97, 98 or 99% identical to said selected sequence.

An aspect of the invention provides a vector comprising the nucleic acid of the invention. An aspect of the invention provides an isolated host cell comprising the vector.

Reference is made to WO2008/096158 for details of library vector systems, combining single variable domains, characterization of dual specific ligands, structure of dual specific ligands, scaffolds for use in constructing dual specific ligands, uses of anti-serum albumin dAbs and multispecific ligands and half-life-enhanced ligands, and compositions and formulations of comprising anti-serum albumin dAbs. These disclosures provide guidance for use with the present invention, including for variants, moieties, ligands, fusion proteins, conjugates, nucleic acids, vectors, hosts and compositions of the present invention.

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DOM7h-11 variant sequences, which are not according to the invention, are disclosed in a co-pending US 2011/0305696 entitled IMPROVED ANTI-SERUM ALBUMIN BINDING VARIANTS, filed on the same day as the present application including (SEQ ID NO:s 1-10).

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SEQUENCES

Table 1: Amino Acid Sequences of DOM7h-14 Variant dAbs

DOM7h-14-10 (SEQ ID NO: 1)

15 DIQMTQSPSSLSASVGDRVTITCRASQWIGSQLSWYQQKPGKAPKLLIMWRSSLQSGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCAQGLRHPKTFGQGTKVEIKR

DOM7h-14-18 (SEQ ID NO:2)

20 DIQMTQSPSSLSASVGDRVTITCRASQWIGSQLSWYQQKPGKAPKLLIMWRSSLQSGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCAQGLMKPMTFGQGTKVEIKR

DOM7h-14-19 (SEQ ID NO: 3)

25 DIQMTQSPSSLSASVGDRVTISCRASQWIGSQLSWYQQKPGKAPKLLIMWRSSLQSGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCAQGAALPRTFGQGTKVEIKR

DOM7h-14-28 (SEQ ID NO: 4)

DIQMTQSPSSLSASVGDRVTITCRASQWIGSQLSWYQQKPGKAPKLLIMWRSSLQSGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCAQGAALPKTFGQGTKVEIKR

30 DOM7h-14-36 (SEQ ID NO: 5)

DIQMTQSPSSLSASVGDRVTITCRASQWIGSQLSWYQQKPGKAPKLLIMWRSSLQSGVP
SRFSGSGSGTDFTLTISLQPEDFATYYCAQGFKKPRTFGQGTKVEIKR

Table 2: Nucleotide Sequences of DOM7h-14 Variant dAbs

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DOM7h-14-10 (SEQ ID NO: 6)

GACATCCAGA TGACCCAGTC TCCATCCTCC CTGTCTGCAT CTGTAGGAGA CCGTGT
CACC ATCACTTGCC GGGCAAGTCA GTGGATTGGG TCTCAGTTAT CTTGGTACCA GC
AGAAACCA GGGAAAGCCC CTAAGCTCCT GATCATGTGG CGTTCCTCGT TGCAAAGT

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GG GGTCCCATCA CGTTTCAGTG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCAT
CAGCAG TCTGCAACCT GAAGATTTTG CTACGTACTA CTGTGCTCAG GGTTTGAGGC
ATCCTAAGAC GTTCGGCCAA GGGACCAAGG TGGAAATCAA ACGG

5 DOM7h-14-18 (SEQ ID NO: 7)

GACATCCAGA TGACCCAGTC TCCATCCTCC CTGTCTGCAT CTGTAGGAGA CCGTGT
CACC ATCACTTGCC GGGCAAGTCA GTGGATTGGG TCTCAGTTAT CTTGGTACCA GC
AGAAACCA GGGAAAGCCC CTAAGCTCCT GATCATGTGG CGTTCCTCGT TGCAAAGT
GG GGTCCCATCA CGTTTCAGTG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCAT
10 CAGCAG TCTGCAACCT GAAGATTTTG CTACGTACTA CTGTGCTCAG GGTCTTATGA
AGCCTATGAC GTTCGGCCAA GGGACCAAGG TGGAAATCAA ACGG

DOM7h-14-19 (SEQ ID NO: 8)

GACATCCAGA TGACCCAGTC TCCATCCTCC CTGTCTGCAT CTGTAGGAGA CCGTGT
15 CACC ATCTCTTGCC GGGCAAGTCA GTGGATTGGG TCTCAGTTAT CTTGGTACCA GC
AGAAACCA GGGGAAGCCC CTAAGCTCCT GATCATGTGG CGTTCCTCGT TGCAAAGT
GG GGTCCCATCA CGTTTCAGTG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCAT
CAGCAG TCTGCAACCT GAAGATTTTG CTACGTACTA CTGTGCTCAG GGTGCGGCGT
TGCCTAGGAC GTTCGGCCAA GGGACCAAGG TGGAAATCAA ACGG

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DOM7h-14-28 (SEQ ID NO: 9)

GACATCCAGA TGACCCAGTC TCCATCCTCC CTGTCTGCAT CTGTAGGAGA CCGTGT
CACC ATCACTTGCC GGGCAAGTCA GTGGATTGGG TCTCAGTTAT CTTGGTACCA GC
AGAAACCA GGGAAAGCCC CTAAGCTCCT GATCATGTGG CGTTCCTCGT TGCAAAGT
25 GG GGTCCCATCA CGTTTCAGTG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCAT
CAGCAG TCTGCAACCT GAAGATTTTG CTACATACTA CTGTGCTCAG GGTGCGGCGT
TGCCTAAGAC GTTCGGCCAA GGGACCAAGG TGGAAATCAA ACGG

DOM7h-14-36 (SEQ ID NO: 10)

GACATCCAGA TGACCCAGTC TCCATCCTCC CTGTCTGCAT CTGTAGGAGA CCGTGT
30 CACC ATCACTTGCC GGGCAAGTCA GTGGATTGGG TCTCAGTTAT CTTGGTACCA GC
AGAAACCA GGGAAAGCCC CTAAGCTCCT GATCATGTGG CGTTCCTCGT TGCAAAGT
GG GGTCCCATCA CGTTTCAGTG GCAGTGGATC TGGGACAGAT TTCACTCTCA CCAT
CAGCAG TCTGCAACCT GAAGATTTTG CTACGTACTA CTGTGCTCAG GGTTTTAAGA
35 AGCCTCGGAC GTTCGGCCAA GGGACCAAGG TGGAAATCAA ACGG

Table 3: Amino Acid Sequences of anti-TNFR1 dAbs

>DOM1h-509 (SEQ ID NO: 11)

EVQLLESGLVQPGGSLRLSCAASGFTFSQYRMHWVRQAPGKSLEWVSSIDTRGSST
40 YYADPVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKAVTMFSPFFDYWGQGLV
TVSS

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>DOM1h-510 (SEQ ID NO: 12)

EVQLLESGGGLVQPGGSLRLSCAASGFTFADYGMWRVRQAPGKGLEWVSSITRTGRVT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKWRNRHGEYLADF DYWGQG
5 TLVTVSS

>DOM1h-543 (SEQ ID NO: 13)

EVQLLESGGGLVQPGGSLRLSCAASGFTFMRYRMHWVRQAPGKGLEWVSSIDSNGSST
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKDRTERS PFVDYWGQGT
10 TVSS

>DOM1h-549 (SEQ ID NO: 14)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVDYEMHWVRQAPGKGLEWVSSISESGTTT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKRRFSASTFDYWGQGT
15 VSS

>DOM1h-574 (SEQ ID NO: 15)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGGHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTGHWEPFDYWGQGT
20 VSS

>DOM1h-574-1 (SEQ ID NO: 16)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGGHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTGRWEPDYWGQGT
25 VSS

>DOM1h-574-2 (SEQ ID NO: 17)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGGHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTGRWEPFDYWGQGT
30 VSS

>DOM1h-574-7 (SEQ ID NO: 18)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGGHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT
35 VSS

>DOM1h-574-8 (SEQ ID NO: 19)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGPEWVSQISNTGGHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT
40 VSS

>DOM1h-574-9 (SEQ ID NO: 20)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGGHT
YYADSVKGRFTISRDN SKNTLYMQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT
45 VSS

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- 5 >DOM1h-574-10 (SEQ ID NO: 21)
EVQLLES GGGGLVQP GGS LRLSCAASGFTFGKY SMGWVRQAPGKDLEWVSQISNTGGHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS
- 10 >DOM1h-574-11 (SEQ ID NO: 22)
EVQLLES GGGGLVQP GGS LRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTGGHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTGRWEPFDHWGQGT LVT
VSS
- 15 >DOM1h-574-12 (SEQ ID NO: 23)
EVQLLES GGGGLVQP GGS LRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTGDHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTGRWEPFDYWGQGT LVT
VSS
- 20 >DOM1h-574-13 (SEQ ID NO: 24)
EVQLLES GGGGLVQP GGS LRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTGRWEPFDYWGQGT LVT
VSS
- 25 >DOM1h-574-14 (SEQ ID NO: 25)
EVQLLES GGGGLVQP GGS LRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS
- 30 >DOM1h-574-15 (SEQ ID NO: 26)
EVQLLES GGGGLVQP GGS LRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTGDHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS
- 35 >DOM1h-574-16 (SEQ ID NO: 27)
EVQLLES GGGGLVQP GGS LRLSCAASGFTFVKY SMGWVRQAPGKGPEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS
- 40 >DOM1h-574-17 (SEQ ID NO: 28)
EVQLLES GGGGLVQP GGS LRLSCAASGFTFVKY SMGWVRQAPGKGPEWVSQISNTGDHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS
- 45 >DOM1h-574-18 (SEQ ID NO: 29)

- 27 -

EVQLLESGGGLVQPGGSLRLSCAASGFTFGKYSMGWVRQAPGKDLEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS

5 >DOM1h-574-19 (SEQ ID NO: 30)

EVQLLESGGGLVQPGGSLRLSCAASGFTFGKYSMGWVRQAPGKDLEWVSQISNTGDHT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS

10 >DOM1h-574-25 (SEQ ID NO: 31)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

15 >DOM1h-574-26 (SEQ ID NO: 32)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFEYWGQGT LVT
VSS

20 >DOM1h-574-27 (SEQ ID NO: 33)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWKPFYWGQGT LVT
VSS

25 >DOM1h-574-28 (SEQ ID NO: 34)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGT LVT
VSS

30 >DOM1h-574-29 (SEQ ID NO: 35)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWRPFYWGQGT LVT
VSS

35 >DOM1h-574-30 (SEQ ID NO: 36)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTGDRR
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAAYYCAIYTGRWEPFDYWGQGT LVT
VSS

40 >DOM1h-574-31 (SEQ ID NO: 37)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRT
YYAHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFNYWGQGT LVT
VSS

45 >DOM1h-574-32 (SEQ ID NO: 38)

- 28 -

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTGDRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

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>DOM1h-574-33 (SEQ ID NO: 39)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTGDRT
10 YYADSVKGRFTISRDN SKNSLYLQMNSLRAEDTAVYYCAIYTGRWVPFDNWGQGLVT
VSS

>DOM1h-574-35 (SEQ ID NO: 40)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFITY SMGWVRQAPGKGLEWVSQISNTGDRT
15 YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFQYWGQGLVT
VSS

>DOM1h-574-36 (SEQ ID NO: 41)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFGKY SMGWVRQAPGKGLEWVSQISNTGDRT
20 YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGLVT
VSS

>DOM1h-574-37 (SEQ ID NO: 42)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFFKY SMGWVRQAPGKGLEWVSQISNTGDRT
25 YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGLVT
VSS

>DOM1h-574-38 (SEQ ID NO: 43)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISDTGDRR
30 YYDDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGLVT
VSS

>DOM1h-574-39 (SEQ ID NO: 44)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTGDRR
35 YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGLVT
VSS

>DOM1h-574-40 (SEQ ID NO: 45)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTGDRT
40 YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFKYWGQGLVT
VSS

>DOM1h-574-53 (SEQ ID NO: 46)

- 29 -

EVQLLESGGGLVQPGGSLRLSCAASGFTFSKYSMGWVRQAPGKGLEWVSQISNTGERR
YYADSVKGRFTISRDNPKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFEYWGQGTLLVT
VSS

5 >DOM1h-574-54 (SEQ ID NO: 47)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVNYSMGWVRQAPGKGLEWVSQISNTGDRT
YYADSVKGRFTISRDNPKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFEYWGQGTLLVT
VTS

10 >DOM1h-574-65 (SEQ ID NO: 48)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTGDRR
YYADSVKGRFTISRDNPKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGTLLVT
VSS

15 >DOM1h-574-66 (SEQ ID NO: 49)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTGDRR
YYADSVKGRFTISRDNPKNTLYLQMNSLRAEDTAVYYCAIYTGRWKPFEYWGQGTLLVT
VSS

20 >DOM1h-574-67 (SEQ ID NO: 50)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTGDRR
YYADSVKGRFTISRDNPKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGTLLVT
VSS

25 >DOM1h-574-68 (SEQ ID NO: 51)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTGDRR
YYADSVKGRFTISRDNPKNTLYLQMNSLRAEDTAVYYCAIYTGRWRPFEYWGQGTLLVT
VSS

30 >DOM1h-574-69 (SEQ ID NO: 52)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTGDRR
YYADSVKGRFTISRDNPKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGTLLVT
VSS

35 >DOM1h-574-70 (SEQ ID NO: 53)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRT
YYAHSVKGRTISRDNPKNTLYLQMNSLRAEDTAVYYCAVYTGRWEPFVYWGQGTLLVT
VSS

40 >DOM1h-574-71 (SEQ ID NO: 54)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRT
YYAHSVKGRTISRDNPKNTLYLQMNSLRAEDTAVYYCAIYTGRWKPFEYWGQGTLLVT
VSS

45 >DOM1h-574-72 (SEQ ID NO: 55)

- 30 -

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTADRT
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGLVT
VSS

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>DOM1h-574-73 (SEQ ID NO: 56)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTADRT
10 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWRPF EYWGQGLVT
VSS

>DOM1h-574-74 (SEQ ID NO: 57)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISNTADRT
15 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-75 (SEQ ID NO: 58)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISDTGDRR
20 YYDDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPF EYWGQGLVT
VSS

>DOM1h-574-76 (SEQ ID NO: 59)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISDTGDRR
25 YYDDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWKPF EYWGQGLVT
VSS

>DOM1h-574-77 (SEQ ID NO: 60)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISDTGDRR
30 YYDDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGLVT
VSS

>DOM1h-574-78 (SEQ ID NO: 61)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISDTGDRR
35 YYDDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWRPF EYWGQGLVT
VSS

>DOM1h-574-79 (SEQ ID NO: 62)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQISDTGDRR
40 YYDDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-84 (SEQ ID NO: 63)

- 31 -

EVQLLES GGG LVQP GGS LRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQISNTGDRR
YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

5 >DOM1h-574-85 (SEQ ID NO: 64)

EVQLLES GGG LVQP GGS LRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQISNTGDRR
YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWKPF EYWGQGT LVT
VSS

10 >DOM1h-574-86 (SEQ ID NO: 65)

EVQLLES GGG LVQP GGS LRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQISNTGDRR
YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPF EYWGQGT LVT
VSS

15 >DOM1h-574-87 (SEQ ID NO: 66)

EVQLLES GGG LVQP GGS LRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQISNTGDRR
YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWRPF EYWGQGT LVT
VSS

20 >DOM1h-574-88 (SEQ ID NO: 67)

EVQLLES GGG LVQP GGS LRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQISNTGDRR
YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPF EYWGQGT LVT
VSS

25 >DOM1h-574-90 (SEQ ID NO: 68)

EVQLLES GGG LVQP GGS LRLSCAASGFTFLKF SMGWVRQAPGKGLEWVSQIANTGDRR
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPF EYWGQGT LVT
VSS

30 >DOM1h-574-91 (SEQ ID NO: 69)

EVQLLES GGG LVQP GGS LRLSCAASGFTFLKYS MGWVRQAPGKGLEWVSQISNTADRT
YYAHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPF EYWGQGT LVT
VSS

35 >DOM1h-574-92 (SEQ ID NO: 70)

EVQLLES GGG LVQP GGS LRLSCAASGFTFFKYS MGWVRQAPGKGLEWVSQISDTGDRR
YYDDSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPF VYWGQGT LVT
VSS

40 >DOM1h-574-93 (SEQ ID NO: 71)

EVQLLES GGG LVQP GGS LRLSCAASGFTFLKYS MGWVRQAPGKGLEWVSQISDTGDRR
YYDDSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPF VYWGQGT LVT
VSS

45 >DOM1h-574-94 (SEQ ID NO: 72)

- 32 -

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQIANTGDRR
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAAYYCAIYTGRWPDFDYWGQGLT
VSS

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>DOM1h-574-95 (SEQ ID NO: 73)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQIANTGDRR
10 YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAAYYCAIYTGRWPDFEYWGQGLT
VSS

>DOM1h-574-96 (SEQ ID NO: 74)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQISNTADRT
15 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWPDFDYWGQGLT
VSS

>DOM1h-574-97 (SEQ ID NO: 75)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQISNTADRT
20 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWPDFEYWGQGLT
VSS

>DOM1h-574-98 (SEQ ID NO: 76)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQISDTGDRR
25 YYDDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWPDFDYWGQGLT
VSS

>DOM1h-574-99 (SEQ ID NO: 77)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYS MGWVRQAPGKGLEWVSQISDTGDRR
30 YYDDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWPDFEYWGQGLT
VSS

>DOM1h-574-100 (SEQ ID NO: 78)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYS MGWVRQAPGKGPEWVSQISAWGDRT
35 YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGLT
VSS

>DOM1h-574-101 (SEQ ID NO: 79)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYS MGWVRQAPGKGPEWVSQISDGGQRT
40 YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGLT
VSS

>DOM1h-574-102 (SEQ ID NO: 80)

- 33 -

EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGPEWVSQISDSGYRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS

5 >DOM1h-574-103 (SEQ ID NO: 81)
EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGPEWVSQISDGGTRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS

10 >DOM1h-574-104 (SEQ ID NO: 82)
EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGPEWVSQISDKGTRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS

15 >DOM1h-574-105 (SEQ ID NO: 83)
EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGPEWVSQISETGRRT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS

20 >DOM1h-574-106 (SEQ ID NO: 84)
EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGLEWVSQINNTGSTT
YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFDYWGQGT LVT
VSS

25 >DOM1h-574-107 (SEQ ID NO: 85)
EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGPEWVSQISNTADRT
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGT LVT
VSS

30 >DOM1h-574-108 (SEQ ID NO: 86)
EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGPEWVSQISNTADRT
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGT LVT
VSS

35 >DOM1h-574-109 (SEQ ID NO: 87)
EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGLEWVSQISDTADRT
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGT LVT
VSS

40 >DOM1h-574-110 (SEQ ID NO: 88)
EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGLEWVSQISDTADRT
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGT LVT
VSS

45 >DOM1h-574-111 (SEQ ID NO: 89)

- 34 -

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
YYDDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWRPF EYWGQGT LVT
VSS

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>DOM1h-574-112 (SEQ ID NO: 90)

10 EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
YYTHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPF EYWGQGT LVT
VSS

>DOM1h-574-113 (SEQ ID NO: 91)

15 EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRR
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPF EYWGQGT LVT
VSS

>DOM1h-574-114 (SEQ ID NO: 92)

20 EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIILNTADRT
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPF EYWGQGT LVT
VSS

>DOM1h-574-115 (SEQ ID NO: 93)

25 EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRT
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPF EYWGQGT LVT
VSS

>DOM1h-574-116 (SEQ ID NO: 94)

30 EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRR
YYAHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPF EYWGQGT LVT
VSS

>DOM1h-574-117 (SEQ ID NO: 95)

35 EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRR
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPF EYWGQGT LVT
VSS

>DOM1h-574-118 (SEQ ID NO: 96)

40 EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRT
YYAHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAVYTGRWVSF EYWGQGT LVT
VSS

>DOM1h-574-119 (SEQ ID NO: 97)

- 35 -

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRT
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCALYTGRWVSFEYWGQGT LVT
VSS

5 >DOM1h-574-120 (SEQ ID NO: 98)
EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRT
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAVYTGRWVPFEYWGQGT LVT
VSS

10 >DOM1h-574-121 (SEQ ID NO: 99)
EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRT
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCALYTGRWVPFEYWGQGT LVT
VSS

15 >DOM1h-574-122 (SEQ ID NO: 100)
EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTADRR
YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGT LVT
VSS

20 >DOM1h-574-123 (SEQ ID NO: 101)
EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRR
YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

25 >DOM1h-574-124 (SEQ ID NO: 102)
EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTGDRR
YYAHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

30 >DOM1h-574-125 (SEQ ID NO: 103)
EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTADRR
YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

35 >DOM1h-574-126 (SEQ ID NO: 104)
EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTGDRR
YYAHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

40 >DOM1h-574-127 (SEQ ID NO: 105)
EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISNTADRR
YYAHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

45 >DOM1h-574-128 (SEQ ID NO: 106)

- 36 -

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTADRR
YYAHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

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>DOM1h-574-129 (SEQ ID NO: 107)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIVNTGDRR
10 YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

>DOM1h-574-130 (SEQ ID NO: 108)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIANTGDRR
15 YYADAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

>DOM1h-574-131 (SEQ ID NO: 109)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
20 YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGT LVT
VSS

>DOM1h-574-132 (SEQ ID NO: 110)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
25 YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWRPF EYWGQGT LVT
VSS

>DOM1h-574-133 (SEQ ID NO: 111)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
30 YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

>DOM1h-574-134 (SEQ ID NO: 112)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
35 YYSHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGT LVT
VSS

>DOM1h-574-135 (SEQ ID NO: 113)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
40 YYTHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGT LVT
VSS

>DOM1h-574-137 (SEQ ID NO: 114)

- 37 -

EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGLEWVSQISDTADRT
YYTDAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

5 >DOM1h-574-138 (SEQ ID NO: 115)
EVQLLES GGG LVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRT
YYAHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGT LVT
VSS

10 >DOM1h-574-139 (SEQ ID NO: 116)
EVQLLES GGG LVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRT
YYAHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGT LVT
VSS

15 >DOM1h-574-140 (SEQ ID NO: 117)
EVQLLES GGG LVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQIADTGDRR
YYDDSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

20 >DOM1h-574-141 (SEQ ID NO: 118)
EVQLLES GGG LVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRR
YYDDSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

25 >DOM1h-574-142 (SEQ ID NO: 119)
EVQLLES GGG LVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTGDRR
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

30 >DOM1h-574-143 (SEQ ID NO: 120)
EVQLLES GGG LVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTGDRR
YYDDAV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

35 >DOM1h-574-144 (SEQ ID NO: 121)
EVQLLES GGG LVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQIADTADRR
YYDDSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

40 >DOM1h-574-145 (SEQ ID NO: 122)
EVQLLES GGG LVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQIADTGDRR
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

45 >DOM1h-574-146 (SEQ ID NO: 123)

- 38 -

EVQLLES GGGGLVQPGGSLRLSCAASGFTFFKYSMGWVRQAPGKGLEWVSQIADTGDRR
YYDDAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

5

>DOM1h-574-147 (SEQ ID NO: 124)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
10 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWGPFVYWGQGT LVT
VSS

>DOM1h-574-148 (SEQ ID NO: 125)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
15 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFAYWGQGT LVT
VSS

>DOM1h-574-149 (SEQ ID NO: 126)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
20 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWGPFQYWGQGT LVT
VSS

>DOM1h-574-150 (SEQ ID NO: 127)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
25 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFQYWGQGT LVT
VSS

>DOM1h-574-151 (SEQ ID NO: 128)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
30 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGT LVT
VSS

>DOM1h-574-152 (SEQ ID NO: 129)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
35 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFQYWGQGT LVT
VSS

>DOM1h-574-153 (SEQ ID NO: 130)

EVQLLES GGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRT
40 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFQYWGQGT LVT
VSS

>DOM1h-574-154 (SEQ ID NO: 131)

- 39 -

EVQLLES GGGGLVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGLEWVSQISDTGDRR
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGT LVT
VSS

5 >DOM1h-574-155 (SEQ ID NO: 132)
EVQLLES GGGGLVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGLEWVSQISDTADRT
YYAHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGT LVT
VSS

10 >DOM1h-574-156 (SEQ ID NO: 133)
EVQLLES GGGGLVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRT
YYAHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGT LVT
VSS

15 >DOM1h-574-157 (SEQ ID NO: 134)
EVQLLES GGGGLVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRT
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWRPFEYWGQGT LVT
VSS

20 >DOM1h-574-158 (SEQ ID NO: 135)
EVQLLES GGGGLVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRT
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWRPFEYWGQGT LVT
VSS

25 >DOM1h-574-159 (SEQ ID NO: 136)
EVQLLES GGGGLVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRT
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

30 >DOM1h-574-160 (SEQ ID NO: 137)
EVQLLES GGGGLVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRT
YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGT LVT
VSS

35 >DOM1h-574-161 (SEQ ID NO: 138)
EVQLLES GGGGLVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRT
YYSHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGT LVT
VSS

40 >DOM1h-574-162 (SEQ ID NO: 139)
EVQLLES GGGGLVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTADRT
YYSHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGT LVT
VSS

45 >DOM1h-574-163 (SEQ ID NO: 140)

- 40 -

EVQLLES GGG LVQP GGS LRLSCAASGFTFFKY SMGWVRQAPGKGLEWVSQISDTADRT
YYTHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGLVT
VSS

5

>DOM1h-574-164 (SEQ ID NO: 141)

EVQLLES GGG LVQP GGS LRLSCAASGFTFLKY SMGWVRQAPGKGLEWVSQISDTADRT
10 YYTHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGLVT
VSS

>DOM1h-574-165 (SEQ ID NO: 142)

EVQLLES GGG LVQP GGS LRLSCAASGFTFFKY SMGWVRQAPGKGLEWVSQISDTADRT
15 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-166 (SEQ ID NO: 143)

EVQLLES GGG LVQP GGS LRLSCAASGFTFLKY SMGWVRQAPGKGLEWVSQISDTADRT
20 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-167 (SEQ ID NO: 144)

EVQLLES GGG LVQP GGS LRLSCAASGFTFLKY SMGWVRQAPGKGLEWVSQISDTGDRR
25 YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-169 (SEQ ID NO: 145)

EVQLLES GGG LVQP GGS LRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQIADTADRT
30 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGLVT
VSS

>DOM1h-574-170 (SEQ ID NO: 146)

EVQLLES GGG LVQP GGS LRLSCAASGFTFFKY SMGWVRQAPGKGLEWVSQISDTADRT
35 YYAHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGLVT
VSS

>DOM1h-574-171 (SEQ ID NO: 147)

EVQLLES GGG LVQP GGS LRLSCAASGFTFVKY SMGWVRQAPGKGLEWVSQIADTADRT
40 YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGLVT
VSS

>DOM1h-574-172 (SEQ ID NO: 148)

- 41 -

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIADTADRT
YYDHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGLVT
VSS

5

>DOM1h-574-173 (SEQ ID NO: 149)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIADTADRR
10 YYAHSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-174 (SEQ ID NO: 150)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRR
15 YYAHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-175 (SEQ ID NO: 151)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIADTADRR
20 YYAHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-176 (SEQ ID NO: 152)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQISDTADRR
25 YYDHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-177 (SEQ ID NO: 153)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIADTADRR
30 YYDHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-178 (SEQ ID NO: 154)

EVQLLESGGGLVQPGGSLRLSCAASGFTFVKYSMGWVRQAPGKGLEWVSQIADTADRR
35 YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
VSS

>DOM1h-574-179 (SEQ ID NO: 155)

EVQLLESGGGLVQPGGSLRLSCAASGFTFFKYSMGWVRQAPGKGLEWVSQISDTADRR
40 YYDDAVKGRFTITRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWEPFVYWGQGLVT
VSS

>DOM1h-574-180 (SEQ ID NO: 156)

- 42 -

EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGLEWVSQISDTADRT
 YYAHAVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWVPFEYWGQGLVT
 VSS

5

>DOM1h-574-4 (SEQ ID NO: 157)

EVQLLES GGG LVQP GGS LRLSCAASGFT FVKYS MGWVRQAPGKGLEWVSQISNTGGHT
 10 YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTGRWEPFEYWGQGLVT
 VSS

>DOM1h-574-168 (SEQ ID NO: 158)

EVQLLES GGG LVQP GGS LRLSCAASGFT FFKYS MGWVRQAPGKGLEWVSQISDTGDRR
 15 YYDHSV KGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAIYTGRWAPFEYWGQGLVT
 VSS

Table 4: Nucleotide sequences of anti-TNFR1 dAbs

20

>DOM1h-509 (SEQ ID NO: 157)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
 TCTCCTGTGCAGCCTCCGGATTACCTTTAGTCAGTATAGGATGCATTGGGTCCGCCA
 GGCTCCAGGGAAGAGTCTAGAGTGGGTCTCAAGTATTGATACTAGGGGTTCGTCTACA
 25 TACTACGCAGACCCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
 GAAAGCTGTGACGATGTTTTCTCCTTTTTTTGACTACTGGGGTCAGGGAACCTTGTC
 ACCGTCTCGAGC

30 >DOM1h-510 (SEQ ID NO: 158)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
 TCTCCTGTGCAGCCTCCGGATTACCTTTGCTGATTATGGGATGCGTTGGGTCCGCCA
 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCATCTATTACGCGGACTGGTTCGTGTTACA
 TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
 35 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
 GAAATGGCGGAATCGGCATGGTGAGTATCTTGCTGATTTTGACTACTGGGGTCAGGGA
 ACCCTGGTCACCGTCTCGAGC

>DOM1h-543 (SEQ ID NO: 159)

40 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
 TCTCCTGTGCAGCCTCCGGATTACCTTTATGAGGTATAGGATGCATTGGGTCCGCCA
 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCATCGATTGATTCTAATGGTTCTAGTACA

- 43 -

TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GAAAGATCGTACGGAGCGTTCGCCGGTTTTTGA CTACTGGGGTCAGGGAACCCTGGTC
ACCGTCTCGAGC

5

>DOM1h-549 (SEQ ID NO: 160)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTGCAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTGATTATGAGATGCATTGGGTCCGCCA
10 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCATCTATTAGTGAGAGTGGTACGACGACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GAAACGTCGTTTTTCTGCTTCTACGTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

15

>DOM1h-574 (SEQ ID NO: 161)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGGTCATACA
20 TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GAAATATACGGGTCATTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

25 >DOM1h-574-1 (SEQ ID NO: 162)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGGTCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
30 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GAAATATACGGGTCGTTGGGAGCCTTATGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

35 >DOM1h-574-2 (SEQ ID NO: 163)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGGTCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
40 GAAATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

45 >DOM1h-574-4 (SEQ ID NO: 164)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA

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GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCTGAATACGGGTGGTCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GAAATATACGGGTCGTTGGGAGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
5 GTCTCGAGC

>DOM1h-574-180 (SEQ ID NO: 165)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
10 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCTGGATACTGCTGATCGTACA
TACTACGCACACGCGGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
15 GTCTCGAGC

>DOM1h-574-7 (SEQ ID NO: 166)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
20 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCTGAATACGGGTGGTCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
25 GTCTCGAGC

>DOM1h-574-8 (SEQ ID NO: 167)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGATGGGTCCGCCA
GGCTCCAGGGAAGGTCCAGAGTGGGTCTCACAGATTTCTGAATACGGGTGGTCATACA
30 TACTACGCAGACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACA
GTCTCGAGC

>DOM1h-574-9 (SEQ ID NO: 168)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCTGAATACGGGTGGTCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTTACCATATCCCGCGACAATTCCAAGAACA
40 CGCTGTATATGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-10 (SEQ ID NO: 169)

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GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGGTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGATCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGGTCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-11 (SEQ ID NO: 170)
10 GAGGTGCAGCTGTTGGAGTCAGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGGTCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
15 GAAATATACGGGTCGTTGGGAGCCTTTTGACCACTGGGGTCAGGGGACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-12 (SEQ ID NO: 171)
20 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
25 GAAATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-13 (SEQ ID NO: 172)
30 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
35 GAAATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-14 (SEQ ID NO: 173)
40 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

45 >DOM1h-574-15 (SEQ ID NO: 174)

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GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-16 (SEQ ID NO: 175)
10 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGATGGGTCCGCCA
GGCTCCAGGGAAGGTCCAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
15 GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACA
GTCTCGAGC

>DOM1h-574-17 (SEQ ID NO: 176)
20 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGATGGGTCCGCCA
GGCTCCAGGGAAGGTCCAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
25 GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACA
GTCTCGAGC

>DOM1h-574-18 (SEQ ID NO: 177)
30 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGATCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
35 GTCTCGAGC

>DOM1h-574-19 (SEQ ID NO: 178)
40 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGATCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCATACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
45 GTCTCGAGC

45 >DOM1h-574-25 (SEQ ID NO: 179)

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GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-26 (SEQ ID NO: 180)
10 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
15 GATATATACGGGTCGTTGGGAGCCTTTTGAAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-27 (SEQ ID NO: 181)
20 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCGGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
25 GATATATACGGGTCGTTGGAAGCCTTTTGAAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-28 (SEQ ID NO: 182)
30 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAAGTACTGGGGTCAGGGAACCCTGGTCACC
35 GTCTCGAGC

>DOM1h-574-29 (SEQ ID NO: 183)
40 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGAGGCCTTTTGAAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

45 >DOM1h-574-30 (SEQ ID NO: 184)

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GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
TACTACGCAGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGCATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGA TACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-31 (SEQ ID NO: 185)
10 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
15 GATATATACGGGTCGTTGGGAGCCTTTTAACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-32 (SEQ ID NO: 186)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
20 TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGCGCCTTTTGA TACTACTGGGGTCAGGGAACCCTGGTCACC
25 GTCTCGAGC

>DOM1h-574-33 (SEQ ID NO: 187)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTTCGATGGGGTGGGTCCGCCA
30 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACT
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGTGCCTTTTGA CAACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-35 (SEQ ID NO: 188)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTATTACGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
40 TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTCA G TACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-36 (SEQ ID NO: 189)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGGTAAGTATTCGATGGGGTGGGTCCGCCA
5 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCGGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-37 (SEQ ID NO: 190)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
15 TACTACGCGAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAAGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-38 (SEQ ID NO: 191)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGGATACGGGTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
25 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-39 (SEQ ID NO: 192)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTAGA
TACTACGCGAGACGCGGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
35 GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-40 (SEQ ID NO: 193)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
40 TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
TACTACGCGAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTAAGTACTGGGGTCAGGGAACCCTGGTCACC
45 GTCTCGAGC

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>DOM1h-574-53 (SEQ ID NO: 194)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTAGTAAGTATTTCGATGGGGTGGGTCCGCCA
5 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGAGCGTAGA
TACTACGCAGACTCAGTGAAGGGCCGGTTCACCATCTCCCGCGACAATCCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGAGCCTTTTGAATACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-54 (SEQ ID NO: 195)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAACTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTACA
15 TACTACGCGGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTATGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCACGAGC

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>DOM1h-574-65 (SEQ ID NO: 196)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
TACTACGCAGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGATAATTCCAAGAACA
25 CACTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-66 (SEQ ID NO: 197)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
TACTACGCAGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
35 GATATATACGGGTCGTTGGAAGCCTTTTGAAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-67 (SEQ ID NO: 198)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
40 TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
TACTACGCAGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAAGTACTGGGGTCAGGGAACCCTGGTCACC
45 GTCTCGAGC

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>DOM1h-574-68 (SEQ ID NO: 199)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
5 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
TACTACGCAGACTCTGTGAAGGGCCGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGAGGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-69 (SEQ ID NO: 200)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
15 TACTACGCAGACTCTGTGAAGGGCCGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-70 (SEQ ID NO: 201)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGTTTACCATCTCCCGCGACAATTCCAAGAACA
25 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GGTATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-71 (SEQ ID NO: 202)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
35 GATATATACGGGTCGTTGGAAGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-72 (SEQ ID NO: 203)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
40 TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
45 GTCTCGAGC

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>DOM1h-574-73 (SEQ ID NO: 204)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
5 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGAGGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-74 (SEQ ID NO: 205)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
15 TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-75 (SEQ ID NO: 206)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGGATACGGGTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
25 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-76 (SEQ ID NO: 207)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCCCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGGATACGGGTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
35 GATATATACGGGTCGTTGGAAGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-77 (SEQ ID NO: 208)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
40 TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGGATACGGGTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
45 GTCTCGAGC

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>DOM1h-574-78 (SEQ ID NO: 209)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
5 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCCGATACGGGTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGAGGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-79 (SEQ ID NO: 210)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCCGATACGGGTGATCGTAGA
15 TACTACGATGACTCTGTGAAGGGCCGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-84 (SEQ ID NO: 211)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCCGAATACGGGTGATCGTAGA
TACTACGACAGACGCGGTGAAGGGGCGTTTACCATCTCCCGCGACAATTCCAAGAACA
25 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-85 (SEQ ID NO: 212)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCCGAATACGGGTGATCGTAGA
TACTACGACAGACGCGGTGAAGGGGCGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
35 GATATATACGGGTCGTTGGAAGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-86 (SEQ ID NO: 213)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
40 TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCCCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCCGAATACGGGTGATCGTAGA
TACTACGACAGACGCGGTGAAGGGGCGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
45 GTCTCGAGC

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- >DOM1h-574-87 (SEQ ID NO: 214)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
5 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTAGA
TACTACGCAGACGCGGTGAAGGGGCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGAGGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC
10
- >DOM1h-574-88 (SEQ ID NO: 215)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGTGATCGTAGA
15 TACTACGCAGACGCGGTGAAGGGGCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC
- >DOM1h-574-90 (SEQ ID NO: 216)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTTTTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
TACTACGCAGACTCTGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
25 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC
- >DOM1h-574-91 (SEQ ID NO: 217)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
35 GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC
- >DOM1h-574-92 (SEQ ID NO: 218)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGGATACGGGTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
45 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC

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GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-93 (SEQ ID NO: 219)

5 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCCGATACGGGTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
10 GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-94 (SEQ ID NO: 220)

15 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
TACTACGCAGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGCATATTACTGTGC
GATATATACGGGTCGGTGGCCCGACTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
20 GTCTCGAGC

>DOM1h-574-95 (SEQ ID NO: 221)

25 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
TACTACGCAGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGCATATTACTGTGC
GATATATACGGGTCGGTGGCCCGACTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
30 GTCTCGAGC

>DOM1h-574-96 (SEQ ID NO: 222)

35 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTGGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGCCCGACTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

40 >DOM1h-574-97 (SEQ ID NO: 223)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTGGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
45 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC

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GATATATACGGGTCGGTGGCCCGACTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-98 (SEQ ID NO: 224)

5 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCCGGATACGGGTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
10 GATATATACGGGTCGGTGGCCCGACTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-99 (SEQ ID NO: 225)

15 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCCGGATACGGGTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGCCCGACTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
20 GTCTCGAGC

>DOM1h-574-100 (SEQ ID NO: 226)

25 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGATGGGTCCGCCA
GGCTCCAGGGAAGGTCCAGAGTGGGTCTCACAGATTTCCGGCTGGGGTGACAGGACA
TACTACGCAGACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
30 GTCTCGAGC

>DOM1h-574-101 (SEQ ID NO: 227)

35 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGTCCAGAGTGGGTCTCACAGATTTCCGACGGCGGTACAGAGGACA
TACTACGCAGACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

40 >DOM1h-574-102 (SEQ ID NO: 228)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGATGGGTCCGCCA
GGCTCCAGGGAAGGTCCAGAGTGGGTCTCACAGATTTCCGACTCCGGTTACCGCACA
TACTACGCAGACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
45 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC

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GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-103 (SEQ ID NO: 229)

5 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCCAGAGTGGGTCTCACAGATTTTCGGACGGGGGTACGCGGACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
10 GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-104 (SEQ ID NO: 230)

15 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGATGGGTCCGCCA
GGCTCCAGGGAAGGTCCAGAGTGGGTCTCACAGATTTTCGGACAAGGGTACGCGCACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
20 GTCTCGAGC

>DOM1h-574-105 (SEQ ID NO: 231)

25 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGATGGGTCCGCCA
GGCTCCAGGGAAGGTCCAGAGTGGGTCTCACAGATTTTCGGAGACCGGTTCGAGGACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
30 GTCTCGAGC

>DOM1h-574-106 (SEQ ID NO: 232)

35 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTAACAATACGGGTTCGACCACA
TACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGACTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

40 >DOM1h-574-107 (SEQ ID NO: 233)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCCAGAGTGGGTCTCACAGATTTTCGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
45 CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC

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GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-108 (SEQ ID NO: 234)

5 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCCAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
10 GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-109 (SEQ ID NO: 235)

15 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
20 GTCTCGAGC

>DOM1h-574-110 (SEQ ID NO: 236)

25 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
30 GTCTCGAGC

>DOM1h-574-111 (SEQ ID NO: 237)

35 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGATGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGAGGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

40 >DOM1h-574-112 (SEQ ID NO: 238)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACACACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
45 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC

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GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-113 (SEQ ID NO: 239)

5 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGCAGA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
10 GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-114 (SEQ ID NO: 240)

15 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
20 GTCTCGAGC

>DOM1h-574-115 (SEQ ID NO: 241)

25 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
30 GTCTCGAGC

>DOM1h-574-116 (SEQ ID NO: 242)

35 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGGATACTGCTGATCGTAGA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

40 >DOM1h-574-117 (SEQ ID NO: 243)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGGATACTGCTGATCGTAGA
TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
45 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC

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GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-118 (SEQ ID NO: 244)

5 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
10 GGTATATACTGGGCGTTGGGTGTCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-119 (SEQ ID NO: 245)

15 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GCTATATACTGGGCGTTGGGTGTCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
20 GTCTCGAGC

>DOM1h-574-120 (SEQ ID NO: 246)

25 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GGTATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
30 GTCTCGAGC

>DOM1h-574-121 (SEQ ID NO: 247)

35 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GCTATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

>DOM1h-574-122 (SEQ ID NO: 248)

45 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACTGCTGATCGTAGA

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TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

5

>DOM1h-574-123 (SEQ ID NO: 249)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTAGA
10 TACTACGCAGACGCGGTGAAGGGGCGGTTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

15

>DOM1h-574-124 (SEQ ID NO: 250)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCGGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACGGGCGATCGTAGA
TACTACGCACACGCGGTGAAGGGGCGGTTTCACCATCTCCCGCGACAATTCCAAGAACA
20 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

25

>DOM1h-574-125 (SEQ ID NO: 251)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTGCGAATACTGCTGATCGTAGA
TACTACGCAGACGCGGTGAAGGGGCGGTTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
30 GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

35

>DOM1h-574-126 (SEQ ID NO: 252)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTGCGAATACGGGTGATCGTAGA
TACTACGCACACGCGGTGAAGGGGCGGTTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

45

>DOM1h-574-127 (SEQ ID NO: 253)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTGAATACTGCTGATCGTAGA

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TACTACGCACACGCGGTGAAGGGGCGGTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

5

>DOM1h-574-128 (SEQ ID NO: 254)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGCTGATCGTAGA
10 TACTACGCACACGCGGTGAAGGGGCGGTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

15

>DOM1h-574-129 (SEQ ID NO: 255)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGTGAATACGGGTGATCGTAGA
TACTACGCAGACGCGGTGAAGGGGCGGTTACCATCTCCCGCGACAATTCCAAGAACA
20 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

25

>DOM1h-574-130 (SEQ ID NO: 256)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGAATACGGGTGATCGTAGA
TACTACGCAGACGCGGTGAAGGGGCGGTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
30 GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

35

>DOM1h-574-131 (SEQ ID NO: 257)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGATCACTCCGTGAAGGGCCGGTTACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

45

>DOM1h-574-132 (SEQ ID NO: 258)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA

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TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGAGGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

5

>DOM1h-574-133 (SEQ ID NO: 259)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
10 TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

15

>DOM1h-574-134 (SEQ ID NO: 260)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACTCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
20 CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

25

>DOM1h-574-135 (SEQ ID NO: 261)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACACACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
30 GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

35

>DOM1h-574-137 (SEQ ID NO: 262)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACACAGACGCGGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

45

>DOM1h-574-138 (SEQ ID NO: 263)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA

- 64 -

TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

5

>DOM1h-574-139 (SEQ ID NO: 264)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
10 TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

15 >DOM1h-574-140 (SEQ ID NO: 265)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
20 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-141 (SEQ ID NO: 266)

25 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTAGA
TACTACGATGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
30 GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-142 (SEQ ID NO: 267)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGCC
35 TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTAGA
TACTACGATCACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAACCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

>DOM1h-574-143 (SEQ ID NO: 268)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
45 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTAGA

- 65 -

TACTACGATGACGCGGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-144 (SEQ ID NO: 269)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACTGCTGATCGTAGA
10 TACTACGATGACTCTGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

15

>DOM1h-574-145 (SEQ ID NO: 270)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACGGGTGATCGTAGA
TACTACGATCACTCTGTGAAGGGCCGGTTCATCTCTCCCGCGACAATTCCAAGAACA
20 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

25

>DOM1h-574-146 (SEQ ID NO: 271)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACGGGTGATCGTAGA
TACTACGATGACGCGGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
30 GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

35

>DOM1h-574-147 (SEQ ID NO: 272)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGGGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
40 GTCTCGAGC

45

>DOM1h-574-148 (SEQ ID NO: 273)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA

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TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGTGCCTTTTGCCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

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>DOM1h-574-149 (SEQ ID NO: 274)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
10 TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGGACCTTTTCAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

15 >DOM1h-574-150 (SEQ ID NO: 275)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
20 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGAGCCTTTTCAGTACTGGGGTCAGGGAACCTCTGGTCACC
GTCTCGAGC

25

>DOM1h-574-151 (SEQ ID NO: 276)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
30 TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGCGCCTTTTGAAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

35 >DOM1h-574-152 (SEQ ID NO: 277)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
40 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGCGCCTTTTCAGTACTGGGGTCAGGGAACCTCTGGTCACC
GTCTCGAGC

>DOM1h-574-153 (SEQ ID NO: 278)

- 67 -

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGTGCCTTTTCAGTACTGGGGTCAGGGCACCCCTGGTCACC
GTCTCGAGC

>DOM1h-574-154 (SEQ ID NO: 279)
10 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATAACCGGTGATCGTAGA
TACTACGATCACTCTGTGAAGGGCCGGTTCACTATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
15 GATATATACGGGTCGTTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-155 (SEQ ID NO: 280)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
20 TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
25 GTCTCGAGC

>DOM1h-574-156 (SEQ ID NO: 281)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
30 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

35 >DOM1h-574-157 (SEQ ID NO: 282)
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
40 TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGAGGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

45 >DOM1h-574-158 (SEQ ID NO: 283)

- 68 -

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGAGGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-159 (SEQ ID NO: 284)

10 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
15 GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-160 (SEQ ID NO: 285)

20 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
25 GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-161 (SEQ ID NO: 286)

30 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACTCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
35 GTCTCGAGC

>DOM1h-574-162 (SEQ ID NO: 287)

40 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACTCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
45 GTCTCGAGC

>DOM1h-574-163 (SEQ ID NO: 288)

- 69 -

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACACACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-164 (SEQ ID NO: 289)

10 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACACACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
15 GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-165 (SEQ ID NO: 290)

20 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
25 GATATATACGGGTCGTTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-166 (SEQ ID NO: 291)

30 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGTTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
35 GTCTCGAGC

>DOM1h-574-167 (SEQ ID NO: 292)

40 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTGAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACCGGTGATCGTAGA
TACTACGATCACTCTGTGAAGGGCCGGTTCATCTCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

45 >DOM1h-574-168 (SEQ ID NO: 293)

- 70 -

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATAACCGGTGATCGTAGA
TACTACGATCACTCTGTGAAGGGCCGGTTCACATCTCTCCGCGACAATTCCAAGAACA
5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-169 (SEQ ID NO: 294)

10 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACTGCTGATCGTACA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCTCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGCGC
15 GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-170 (SEQ ID NO: 295)

20 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTTTTAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTTCGGATACTGCTGATCGTACA
TACTACGCACACGCGGTGAAGGGCCGGTTCACCATCTCTCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
25 GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-171 (SEQ ID NO: 296)

30 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTGCAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACTGCTGATCGTACA
TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCTCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
35 GTCTCGAGC

>DOM1h-574-172 (SEQ ID NO: 297)

40 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACTGCTGATCGTACA
TACTACGATCACGCGGTGAAGGGCCGGTTCACCATCTCTCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCTGAGGACACCGCGGTATATTACTGTGC
GATATATACTGGGCGTTGGGTGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
45 GTCTCGAGC

>DOM1h-574-173 (SEQ ID NO: 298)

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GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACTGCTGATCGTAGA
TACTACGCACACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-174 (SEQ ID NO: 299)

10 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCGGATACTGCTGATCGTAGA
TACTACGCACACGCGGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
15 GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-175 (SEQ ID NO: 300)

20 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACTGCTGATCGTAGA
TACTACGCACACGCGGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
25 GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
GTCTCGAGC

>DOM1h-574-176 (SEQ ID NO: 301)

30 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCGGATACTGCTGATCGTAGA
TACTACGATCACGCGGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGAACCCTGGTCACC
35 GTCTCGAGC

>DOM1h-574-177 (SEQ ID NO: 302)

40 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTTCGATGGGGTGGGTCCGCCA
GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACTGCTGATCGTAGA
TACTACGATCACGCGGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
GATATATACGGGTCGGTGGGCGCCTTTTGAGTACTGGGGTCAGGGGACCCTGGTCACC
45 GTCTCGAGC

>DOM1h-574-178 (SEQ ID NO: 303)

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GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
 TCTCCTGTGCAGCCTCCGGATTACCTTTGTAAAGTATTCGATGGGGTGGGTCCGCCA
 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTGCGGATACTGCTGATCGTAGA
 TACTACGATCACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGACAATTCCAAGAACA
 5 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
 GATATATACGGGTCGGTGGGCGCCTTTTGTAGTACTGGGGTCAGGGAACCCTGGTCACC
 GTCTCGAGC

>DOM1h-574-179 (SEQ ID NO: 304)
 10 GAGGTGCAGCTGCTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGCGTC
 TCTCCTGTGCAGCCTCCGGATTACCTTTTCAAGTATTCGATGGGGTGGGTCCGCCA
 GGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACAGATTTCGGATACTGCTGATCGTAGA
 TACTACGATGACGCGGTGAAGGGCCGGTTCACCATCACCCGCGACAATTCCAAGAACA
 CGCTGTATCTGCAAATGAACAGCCTGCGTGCCGAGGACACCGCGGTATATTACTGTGC
 15 GATATATACGGGTCGTTGGGAGCCTTTTGTCTACTGGGGTCAGGGAACCCTGGTCACC
 GTCTCGAGC

Table 5: Anti-serum albumin dAb (DOM7h) fusions

20

(used in Rat studies):-

DOM7h-14/Exendin-4 fusion

DMS number 7138

25 Amino acid sequence (SEQ ID NO: 305)

HGEGTFTSDLSKQMEEEA VRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGGG
 GSDIQMTQSPSSLSASVGDRVTITCRASQWIGSQLSWYQQKPGKAPKLLIMWRS
 SLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQGAALPRTFGQGTKVEIK
 30 R

Nucleotide sequence (SEQ ID NO: 306)

CATGGTGAAGGAACATTTACCAGTGACTTGTCAAAACAGATGGAAGAGGAG
 35 GCAGTGCGGTTATTTATTGAGTGGCTTAAGAACGGAGGACCAAGTAGCGGG
 GCACCTCCGCCATCGGGTGGTGGAGGCGGTTACGGCGGAGGTGGCAGCGGC
 GGTGGCGGGTTCGGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCAT
 CTGTAGGAGACCGTGTCAACATCACTTGCCGGGCAAGTCAGTGGATTGGGT
 CTCAGTTATCTTGGTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA
 40 TCATGTGGCGTTCCTCGTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAG
 TGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGAT
 TTTGCTACGTACTACTGTGCTCAGGGTGCGGCGTTGCCTAGGACGTTTCGGCC
 AAGGGACCAAGGTGGAAATCAAACGG

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DOM7h-14-10/Exendin-4 fusion DMS number 7139

Amino acid sequence (SEQ ID NO: 307)

5

HGEGTFTSDLSKQMEEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGGG
 GSDIQMTQSPSSLSASVGDRVITITCRASQWIGSQLSWYQQKPGKAPKLLIMWRS
 SLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCAQGLRHPKTFGQGTKVEIK
 R

10

Nucleotide sequence (SEQ ID NO: 308)

CATGGTGAAGGAACATTTACCACTGACTTGTCAAAACAGATGGAAGAGGAG
 GCAGTGCGGTTATTTATTGAGTGGCTTAAGAACGGAGGACCAAGTAGCGGG
 15 GCACCTCCGCCATCGGGTGGTGGAGGCGGTTTCAGGCGGAGGTGGCAGCGGC
 GGTGGCGGGTCGGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCAT
 CTGTAGGAGACCGTGTCACCATCACTTGCCGGGCAAGTCAGTGGATTGGGT
 CTCAGTTATCTTGGTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA
 TCATGTGGCGTTCCCTCGTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAG
 20 TGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGAT
 TTTGCTACGTACTACTGTGCTCAGGGTTTGAGGCATCCTAAGACGTTTCGGCC
 AAGGGACCAAGGTGGAAATCAAACGG

25 DOM7h-14-18/Exendin-4 fusion DMS number 7140

Amino acid sequence (SEQ ID NO: 309)

HGEGTFTSDLSKQMEEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGGG
 30 GSDIQMTQSPSSLSASVGDRVITITCRASQWIGSQLSWYQQKPGKAPKLLIMWRS
 SLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCAQGLMKPMTFGQGTKVEIK
 R

Nucleotide sequence (SEQ ID NO: 310)

35

CATGGTGAAGGAACATTTACCACTGACTTGTCAAAACAGATGGAAGAGGAG
 GCAGTGCGGTTATTTATTGAGTGGCTTAAGAACGGAGGACCAAGTAGCGGG
 GCACCTCCGCCATCGGGTGGTGGAGGCGGTTTCAGGCGGAGGTGGCAGCGGC
 GGTGGCGGGTCGGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCAT
 40 CTGTAGGAGACCGTGTCACCATCACTTGCCGGGCAAGTCAGTGGATTGGGT
 CTCAGTTATCTTGGTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA
 TCATGTGGCGTTCCCTCGTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAG
 TGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGAT
 TTTGCTACGTACTACTGTGCTCAGGGTCTTATGAAGCCTATGACGTTTCGGCC
 45 AAGGGACCAAGGTGGAAATCAAACGG

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DOM7h-14-19/Exendin-4 fusion DMS number 7141

5 Amino acid sequence (SEQ ID NO: 311)

HGEGTFTSDLKQMEEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGGG
 GSDIQMTQSPSSLASVGDRVTISCRASQWIGSQLSWYQQKPGEAPKLLIMWRS
 SLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCAQGAALPRTFGQGTKVEIK

10 R

Nucleotide sequence (SEQ ID NO: 312)

CATGGTGAAGGAACATTTACCAGTGACTTGTCAAAACAGATGGAAGAGGAG
 15 GCAGTGCGGTTATTTATTGAGTGGCTTAAGAACGGAGGACCAAGTAGCGGG
 GCACCTCCGCCATCGGGTGGTGGAGGCGGTTTCAGGCGGAGGTGGCAGCGGC
 GGTGGCGGGTCGGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCAT
 CTGTAGGAGACCGTGTCAACATCTCTTGCCGGGCAAGTCAGTGGATTGGGTC
 TCAGTTATCTTGGTACCAGCAGAAACCAGGGGAAGCCCCTAAGCTCCTGAT
 20 CATGTGGCGTTCCTCGTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAGT
 GGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATT
 TTGCTACGTACTACTGTGCTCAGGGTGCGGCGTTGCCTAGGACGTTCCGCCA
 AGGGACCAAGGTGGAAATCAAACGG

25 **DOM7h-11/Exendin-4 fusion DMS number 7142**

Amino acid sequence (SEQ ID NO: 313)

HGEGTFTSDLKQMEEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGGG
 30 GSDIQMTQSPSSLASVGDRVTITCRASRPIGTTLSWYQQKPGKAPKLLIWFGSR
 LQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCAQAGTHPTTFGQGTKVEIKR

Nucleotide sequence (SEQ ID NO: 314)

35 CATGGTGAAGGAACATTTACCAGTGACTTGTCAAAACAGATGGAAGAGGAG
 GCAGTGCGGTTATTTATTGAGTGGCTTAAGAACGGAGGACCAAGTAGCGGG
 GCACCTCCGCCATCGGGTGGTGGAGGCGGTTTCAGGCGGAGGTGGCAGCGGC
 GGTGGCGGGTCGGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCAT
 40 CTGTAGGAGACCGTGTCAACATCACTTGCCGGGCAAGTCGTCCGATTGGGA
 CGACGTAAAGTTGGTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA
 TCTGGTTTGGTTCCCGGTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAG
 TGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGAT
 TTTGCTACGTACTACTGTGCGCAGGCTGGGACGCATCCTACGACGTTCCGGCC
 45 AAGGGACCAAGGTGGAAATCAAACGG

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DOM7h-11-12/Exendin-4 fusion DMS number 7147

Amino acid sequence (SEQ ID NO: 315)

5

HGEGTFTSDLSKQMEEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGGG
GSDIQMTQSPSSLSASVGDRVITTCRASRPIGTMLSWYQQKPGKAPKLLILFGR
LQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQAGTHPTTFGQGTKVEIKR

10

Nucleotide sequence (SEQ ID NO: 316)

15

CATGGTGAAGGAACATTTACCAGTGACTTGTCAAAACAGATGGAAGAGGAG
GCAGTGCGGTTATTTATTGAGTGGCTTAAGAACGGAGGACCAAGTAGCGGG
GCACCTCCGCCATCGGGTGGTGGAGGCGGTTTCAGGCGGAGGTGGCAGCGGC
GGTGGCGGGTCGGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCAT
20 CTGTAGGAGACCGTGTCAACATCACTTGCCGGGCAAGTCGTCCGATTGGGA
CGATGTTAAGTTGGTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA
TCTTGTGTTGGTTCCCGTTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAG
TGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGAT
TTTGCTACGTACTACTGTGCGCAGGCTGGGACGCATCCTACGACGTTTCGGCC
25 AAGGGACCAAGGTGGAAATCAAACGG

DOM7h-11-15/Exendin-4 fusion DMS number 7143

Amino acid sequence (SEQ ID NO: 317)

30

HGEGTFTSDLSKQMEEEEAVRLFIEWLKNGGPSSGAPPPSGGGGGSGGGGSGGG
GSDIQMTQSPSSLSASVGDRVITTCRASRPIGTMLSWYQQKPGKAPKLLILAFSR
LQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCAQAGTHPTTFGQGTKVEIKR

35

Nucleotide sequence (SEQ ID NO: 318)

CATGGTGAAGGAACATTTACCAGTGACTTGTCAAAACAGATGGAAGAGGAG
GCAGTGCGGTTATTTATTGAGTGGCTTAAGAACGGAGGACCAAGTAGCGGG
40 GCACCTCCGCCATCGGGTGGTGGAGGCGGTTTCAGGCGGAGGTGGCAGCGGC
GGTGGCGGGTCGGACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCAT
CTGTAGGAGACCGTGTCAACATCACTTGCCGGGCAAGTCGTCCGATTGGGA
CGATGTTAAGTTGGTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGA
TCCTTGCTTTTTCCCGTTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAGT
45 GGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATT

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TTGCTACGTACTACTGCGCGCAGGCTGGGACGCATCCTACGACGTTTCGGCCA
AGGGACCAAGGTGGAAATCAAACGG

5 **DOM7h14-10/ G4SC-NCE fusion**

Amino acid sequence (SEQ ID NO: 319) encoding DOM7h14-10/G4SC

10 DIQMTQSPSSLSASVGDRVTITCRASQWIGSQLSWYQQKPGKAPKLLIMWRSSL
QSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCAQGLRHPKTFGQGTKVEIKRG
GGGSC

15 The C-terminal cysteine can be linked to a new chemical entity (pharmaceutical
chemical compound, NCE), eg using maleimide linkage.

Nucleotide sequence (SEQ ID NO: 320) encoding DOM7h14-10/G4SC

20 GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACC
GTGTCACCATCACTTGCCGGGCAAGTCAGTGGATTGGGTCTCAGTTATCTTG
GTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCATGTGGCGTTC
CTCGTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAGTGGATCTGGGAC
AGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCTACGTAC
TACTGTGCTCAGGGTTTGAGGCATCCTAAGACGTTTCGGCCAAGGGACCAAG
25 GTGGAAATCAAACGGGGTGGCGGAGGGGGTTCCTGT

DOM7h14-10/TVAAPSC fusion

30 Amino acid sequence (SEQ ID NO: 321)

DIQMTQSPSSLSASVGDRVTITCRASQWIGSQLSWYQQKPGKAPKLLIMWRSSL
QSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCAQGLRHPKTFGQGTKVEIKRT
VAAPSC

35 The C-terminal cysteine can be linked to a new chemical entity (pharmaceutical
chemical compound, NCE), eg using maleimide linkage.

Nucleotide sequence (SEQ ID NO: 322)

40 GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACC
GTGTCACCATCACTTGCCGGGCAAGTCAGTGGATTGGGTCTCAGTTATCTTG
GTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCATGTGGCGTTC
CTCGTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAGTGGATCTGGGAC
AGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCTACGTAC
45 TACTGTGCTCAGGGTTTGAGGCATCCTAAGACGTTTCGGCCAAGGGACCAAG

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GTGGAAATCAAACGGACCGTCGCTGCTCCATCTTGT

5

10 (used in mouse studies):-

DOM7h-11/DOM1m-21-23 fusion**DMS number 5515**

Amino acid sequence (SEQ ID NO: 323)

15

EVQLLES GGGLVQPGGSLRLSCAASGFTFNRYSMGWLRQAPGKGLEWVSRIDS
 YGRGTYIEDPVKGRFSISRDN SKNTLYLQMNSLRAEDTAVYYCAKISQFGSNA
 FDYWGQGTQVTVSSASTSGPSDIQMTQSPSSLSASVGDRVITICRASRPIGTTLS
 WYQQKPGKAPKLLIWFGSRLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYC
 20 AQAGTHPTTFGQGTKVEIKR

Amino acid plus nucleotide plus myc tag sequence (SEQ ID NO: 324)

25

EVQLLES GGGLVQPGGSLRLSCAASGFTFNRYSMGWLRQAPGKGLEWVSRIDS
 YGRGTYIEDPVKGRFSISRDN SKNTLYLQMNSLRAEDTAVYYCAKISQFGSNA
 FDYWGQGTQVTVSSASTSGPSDIQMTQSPSSLSASVGDRVITICRASRPIGTTLS
 WYQQKPGKAPKLLIWFGSRLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYC
 AQAGTHPTTFGQGTKVEIKRAAAEQKLISEEDLN

30 Nucleotide sequence (SEQ ID NO: 325)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCC
 CTGCGTCTCTCCTGTGCAGCCTCCGGATTACCTTTAATAGGTATAGTATGG
 GGTGGCTCCGCCAGGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACGGATTG
 35 ATTCTTATGGTCGTGGTACATACTACGAAGACCCCGTGAAGGGCCGGTTCA
 GCATCTCCCGCGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCC
 TGCGTGCCGAGGACACCGCCGTATATTACTGTGCGAAAATTTCTCAGTTTGG
 GTCAAATGCGTTTGACTACTGGGGTCAGGGAACCCAGGTACCGTCTCGAG
 CGCTAGCACCAAGTGGTCCATCGGACATCCAGATGACCCAGTCTCCATCCTCC
 40 CTGTCTGCATCTGTAGGAGACCGTGTCAACCATCACTTGCCGGGCAAGTCGTC
 CGATTGGGACGACGTTAAGTTGGTACCAGCAGAAACCAGGGAAAGCCCCTA
 AGCTCCTGATCTGGTTTGGTTCCCGGTTGCAAAGTGGGGTCCCATCACGTTT
 CAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA
 ACCTGAAGATTTTGCTACGTACTACTGTGCGCAGGCTGGGACGCATCCTACG
 45 ACGTTCGGCCAAGGGACCAAGGTGGAAATCAAACGG

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Nucleotide plus myc tag sequence (SEQ ID NO: 326)

5 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCC
 CTGCGTCTCTCCTGTGCAGCCTCCGGATTACCTTTAATAGGTATAGTATGG
 GGTGGCTCCGCCAGGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACGGATTG
 ATTCTTATGGTCGTGGTACATACTACGAAGACCCCGTGAAGGGCCGGTTCA
 GCATCTCCCGCGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCC
 10 TCGTGCCGAGGACACCGCCGTATATTACTGTGCGAAAATTTCTCAGTTTGG
 GTCAAATGCGTTTGACTACTGGGGTCAGGGAACCCAGGTCACCGTCTCGAG
 CGCTAGCACCAGTGGTCCATCGGACATCCAGATGACCCAGTCTCCATCCTCC
 CTGTCTGCATCTGTAGGAGACCGTGTACCATCACTTGCCGGGCAAGTCGTC
 CGATTGGGACGACGTTAAGTTGGTACCAGCAGAAACCAGGGAAAGCCCCTA
 AGCTCCTGATCTGGTTTGGTTCCCGGTTGCAAAGTGGGGTCCCATCACGTTT
 15 CAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA
 ACCTGAAGATTTTGCTACGTACTACTGTGCGCAGGCTGGGACGCATCCTACG
 ACGTTCGGCCAAGGGACCAAGGTGGAAATCAAACGGGCGGCCGCAGAACAA
 AAAACTCATCTCAGAAGAGGATCTGAATTAA
 20

DOM7h-11-12/DOM1m-21-23 fusion DMS number 5516

Amino acid sequence (SEQ ID NO: 327)

25 EVQLLES GGGLVQPGGSLRLSCAASGFTFNRYSMGWLRQAPGKGLEWVSRIDS
 YGRGTYIEDPVKGRFSISRDN SKNTLYLQMNSLRAEDTAVYYCAKISQFGSNA
 FDYWGQGTQVTVSSASTSGPSDIQMTQSPSSLSASVGDRVTITCRASRPIGTMLS
 30 WYQQKPGKAPKLLILFGSRLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCA
 QAGTHPTTFGQGTKVEIKR

Amino acid plus nucleotide plus myc tag sequence (SEQ ID NO: 328)

35 EVQLLES GGGLVQPGGSLRLSCAASGFTFNRYSMGWLRQAPGKGLEWVSRIDS
 YGRGTYIEDPVKGRFSISRDN SKNTLYLQMNSLRAEDTAVYYCAKISQFGSNA
 FDYWGQGTQVTVSSASTSGPSDIQMTQSPSSLSASVGDRVTITCRASRPIGTMLS
 WYQQKPGKAPKLLILFGSRLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCA
 QAGTHPTTFGQGTKVEIKRAAAEQKLISEEDLN

40 Nucleotide sequence (SEQ ID NO: 329)

45 GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCC
 CTGCGTCTCTCCTGTGCAGCCTCCGGATTACCTTTAATAGGTATAGTATGG
 GGTGGCTCCGCCAGGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACGGATTG
 ATTCTTATGGTCGTGGTACATACTACGAAGACCCCGTGAAGGGCCGGTTCA

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GCATCTCCCGCGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCC
 TGCGTGCCGAGGACACCGCCGTATATTACTGTGCGAAAATTTCTCAGTTTGG
 GTCAAATGCGTTTGACTIONTGGGGTCAGGGAACCCAGGTCACCGTCTCGAG
 CGCTAGCACCAGTGGTCCATCGGACATCCAGATGACCCAGTCTCCATCCTCC
 5 CTGTCTGCATCTGTAGGAGACCGTGTCAACATCACTTGCCGGGCAAGTCGTC
 CGATTGGGACGATGTTAAGTTGGTACCAGCAGAAACCAGGGAAAGCCCCTA
 AGCTCCTGATCTTGTGTTGGTTCCCGGTTGCAAAGTGGGGTCCCATCACGTTT
 CAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA
 ACCTGAAGATTTTGCTACGTACTACTGTGCGCAGGCTGGGACGCATCCTACG
 10 ACGTTCGGCCAAGGGACCAAGGTGGAAATCAAACGG

Nucleotide plus myc tag sequence (SEQ ID NO: 330)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCC
 15 CTGCGTCTCTCCTGTGCAGCCTCCGGATTACCTTTAATAGGTATAGTATGG
 GGTGGCTCCGCCAGGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACGGATTG
 ATTCTTATGGTCGTGGTACATACTACGAAGACCCCGTGAAGGGCCGGTTCA
 GCATCTCCCGCGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCC
 TGCGTGCCGAGGACACCGCCGTATATTACTGTGCGAAAATTTCTCAGTTTGG
 20 GTCAAATGCGTTTGACTIONTGGGGTCAGGGAACCCAGGTCACCGTCTCGAG
 CGCTAGCACCAGTGGTCCATCGGACATCCAGATGACCCAGTCTCCATCCTCC
 CTGTCTGCATCTGTAGGAGACCGTGTCAACATCACTTGCCGGGCAAGTCGTC
 CGATTGGGACGATGTTAAGTTGGTACCAGCAGAAACCAGGGAAAGCCCCTA
 AGCTCCTGATCTTGTGTTGGTTCCCGGTTGCAAAGTGGGGTCCCATCACGTTT
 25 CAGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCA
 ACCTGAAGATTTTGCTACGTACTACTGTGCGCAGGCTGGGACGCATCCTACG
 ACGTTCGGCCAAGGGACCAAGGTGGAAATCAAACGGGCGGCCGCAGAACAA
 AAAACTCATCTCAGAAGAGGATCTGAATTAA

30

DOM7h-11-15/DOM1m-21-23 fusion DMS number 5517

Amino acid sequence (SEQ ID NO: 331)

35 EVQLLES GGGLVQP GGSRLRLSCAASGFTFNRYSMGWLRQAPGKGLEWVSRIDS
 YGRGTYIEDPVKGRFSISRDN SKNTLYLQMNSLRAEDTAVYYCAKISQFGSNA
 FDYWGQGTQVTVSSASTSGPSDIQMTQSPSSLSASVGD RVTITCRASRPIGTMLS
 WYQQKPGKAPKLLILAFSRLQSGVPSRFS GSGSGTDFTLTIS SLQPEDFATYYCA
 QAGTHPTTFGQGTKVEIKR

40

Amino acid plus nucleotide plus myc tag sequence (SEQ ID NO: 332)

EVQLLES GGGLVQP GGSRLRLSCAASGFTFNRYSMGWLRQAPGKGLEWVSRIDS
 45 YGRGTYIEDPVKGRFSISRDN SKNTLYLQMNSLRAEDTAVYYCAKISQFGSNA
 FDYWGQGTQVTVSSASTSGPSDIQMTQSPSSLSASVGD RVTITCRASRPIGTMLS

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WYQQKPGKAPKLLILAFSRLQSGVPSRFSGSGSDFTLTISSLQPEDFATYYCA
QAGTHPTTFGQGTKVEIKRAAAEQKLISEEDLN

Nucleotide sequence (SEQ ID NO: 333)

5

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCC
CTGCGTCTCTCCTGTGCAGCCTCCGGATTACCTTTAATAGGTATAGTATGG
GGTGGCTCCGCCAGGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACGGATTG
ATTCTTATGGTCGTGGTACATACTACGAAGACCCCGTGAAGGGCCGGTTCA
10 GCATCTCCCGCGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCC
TGCGTGCCGAGGACACCGCCGTATATTACTGTGCGAAAATTTCTCAGTTTGG
GTCAAATGCGTTTGACTACTGGGGTCAGGGAACCCAGGTACACGTCTCGAG
CGCTAGCACCAGTGGTCCATCGGACATCCAGATGACCCAGTCTCCATCCTCC
CTGTCTGCATCTGTAGGAGACCGTGTCAACCATCACTTGCCGGGCAAGTCGTC
15 CGATTGGGACGATGTTAAGTTGGTACCAGCAGAAACCAGGGAAAGCCCCTA
AGCTCCTGATCCTTGCTTTTTCCCGTTTGCAAAGTGGGGTCCCATCACGTTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAA
CCTGAAGATTTTGCTACGTACTACTGCGCGCAGGCTGGGACGCATCCTACGA
CGTTCGGCCAAGGGACCAAGGTGGAAATCAAACGG

20

Nucleotide plus myc tag sequence (SEQ ID NO: 334)

GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCC
CTGCGTCTCTCCTGTGCAGCCTCCGGATTACCTTTAATAGGTATAGTATGG
25 GGTGGCTCCGCCAGGCTCCAGGGAAGGGTCTAGAGTGGGTCTCACGGATTG
ATTCTTATGGTCGTGGTACATACTACGAAGACCCCGTGAAGGGCCGGTTCA
GCATCTCCCGCGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCC
TGCGTGCCGAGGACACCGCCGTATATTACTGTGCGAAAATTTCTCAGTTTGG
GTCAAATGCGTTTGACTACTGGGGTCAGGGAACCCAGGTACACGTCTCGAG
30 CGCTAGCACCAGTGGTCCATCGGACATCCAGATGACCCAGTCTCCATCCTCC
CTGTCTGCATCTGTAGGAGACCGTGTCAACCATCACTTGCCGGGCAAGTCGTC
CGATTGGGACGATGTTAAGTTGGTACCAGCAGAAACCAGGGAAAGCCCCTA
AGCTCCTGATCCTTGCTTTTTCCCGTTTGCAAAGTGGGGTCCCATCACGTTTC
AGTGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAA
35 CCTGAAGATTTTGCTACGTACTACTGCGCGCAGGCTGGGACGCATCCTACGA
CGTTCGGCCAAGGGACCAAGGTGGAAATCAAACGGGCGGCCGCAGAACAA
AAACTCATCTCAGAAGAGGATCTGAATTAA

40

where a myc-tagged molecule is indicated in this table, this was the version used in PK studies in the examples. Where no myc-tagged sequences are given, the PK studies in the examples were not done with myc-tagged material, ie, the studies were done with

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the non-tagged constructs shown.

EXEMPLIFICATION

- 5 All numbering in the experimental section is according to Kabat (Kabat, E.A. National Institutes of Health (US) & Columbia University. Sequences of proteins of immunological interest, edn 5 (US Dept. Of Health and Human Services Public Health Service, National Institutes of Health, Bethesda, MD, 1991)).
- 10 Derivation of DOM7h-11 and DOM7h-14 variants is described. DOM7h-11 variants are not according to the invention.

EXAMPLE 1: Vk Affinity Maturation

- 15 **Selections:**
HSA (Human Serum Albumin) and RSA (Rat Serum Albumin) antigens were obtained from Sigma (essentially fatty acid free, ~99% (agarose gel electrophoresis), lyophilized powder Cat. No. A3782 and A6414 respectively)
- 20 Biotinylated products of above two antigens were made by using EZ Link^{*} Sulfo-NHS-SS-Biotin (Pierce, Cat. No.21331). Free biotin reagent was removed by passing the samples twice through PD10 desalting column followed by overnight dialysis against 1000x excess volume of PBS at 4°C. Resulting product was tested by mass spec and 1-2 biotins per molecule were observed.
- 25 **Affinity maturation libraries:**
Both error-prone and CDR libraries were created using DOM7h-11 and DOM7h-14 parental dAbs (see WO2008/096158 for the sequences of DOM7h-11 and DOM7h-14). The CDR libraries were generated in the pDOM4 vector and the error prone libraries
- 30 were generated in the pDOM33 vector (to allow for selection with or without protease

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- treatment). Vector pDOM4, is a derivative of the Fd phage vector in which the *gene III* signal peptide sequence is replaced with the yeast glycolipid anchored surface protein (GAS) signal peptide. It also contains a *c-myc* tag between the leader sequence and *gene III*, which puts the *gene III* back in frame. This leader sequence functions well both in
- 5 phage display vectors but also in other prokaryotic expression vectors and can be universally used. pDOM33 is a modified version of the pDOM4 vector where the the *c-myc* tag has been removed which renders the dAb-phage fusion resistant to the protease trypsin. This allows the use of trypsin within the phage selection to select for dAbs that are more protease stable (see WO2008149143).
- 10 For error-prone maturation libraries, plasmid DNA encoding the dAb to be matured was amplified by PCR, using the GENEMORPH[®] II RANDOM MUTAGENESIS KIT (random, unique mutagenesis kit, Stratagene). The product was digested with *Sal* I and *Not* I and used in a ligation reaction with cut phage vector pDOM33.
- 15 For the CDR libraries, PCR reactions were performed using degenerate oligonucleotides containing NNK or NNS codons to diversify the required positions in the dAb to be affinity matured. Assembly PCR was then used to generate a full length diversified insert. The insert was digested with *Sal* I and *Not* I and used in a ligation reaction with pDOM4 for mutagenesis of multiple residues and pDOM5 for
- 20 mutagenesis of single residues. The pDOM5 vector is a pUC119-based expression vector where protein expression is driven by the LacZ promoter. A GAS1 leader sequence (see WO 2005/093074) ensures secretion of isolated, soluble dAbs into the periplasm and culture supernatant of *E. coli*. dAbs are cloned *Sal*I/*Not*I in this vector, which appends a myc tag at the C-terminus of the dAb. This protocol using *Sal*I and
- 25 *Not* I results in inclusion of an ST amino acid sequence at the N-terminus.

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The ligation produced by either method was then used to transform *E. coli* strain TB1 by electroporation and the transformed cells plated on 2xTY agar containing 15 µg/ml tetracycline, yielding library sizes of $>5 \times 10^7$ clones.

5

The error-prone libraries had the following average mutation rate and size: DOM7h-11 (2.5 mutations per dAb), size: 6.1×10^8 , DOM7h-14 (2.9 mutations per dAb), size: 5.4×10^8 .

- 10 Each CDR library has four amino acid diversity. Two libraries were generated for each of CDRs 1 and 3, and one library for CDR2. The positions diversified within each library are as follows (amino acids based on VK dummy DPK9 sequence):

		Library size	
		DOM7h-11	DOM7h-14
15	1 – Q27, S28, S30, S31 (CDR1)	8.8×10^7	5.8×10^7
	2 – S30, S31, Y32, N34 (CDR1)	4.6×10^8	4.2×10^8
	3 – Y49, A50, A51, S53 (CDR2)	3.9×10^8	2.4×10^8
	4 – Q89, S91, Y92, S93 (CDR3)	1.8×10^8	2.5×10^8
	5 – Y92, Y93, T94, N96 (CDR3)	4.0×10^8	3.3×10^8

20

Example 2: Selection strategies:

Three phage selection strategies were adopted for Vκ AlbudAb™ (anti-serum albumin dAb) affinity maturation:

- 25 1) Selections against HSA only:

Three rounds of selection against HSA were carried out. The error prone libraries and each CDR library were selected as an individual pool in all rounds. The first round of selection was performed against HSA passively coated onto an immunotube at 1mg/ml. Round 2 was performed against 100nM HSA and round 3
30 against 10nM (CDR selections) or 20 or 100nM (Error prone selections) HSA, both

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as soluble selections followed by a fourth round of selection with the error prone libraries against 1.5 nM HSA as a soluble selection. The error prone libraries were eluted with 0.1M glycine pH 2.0 before neutralisation with 1M Tris pH 8.0 and the CDR libraries were eluted with 1mg/ml trypsin before infection into log phase TG1
5 cells. The third round of each selection was subcloned into pDOM5 for screening. Soluble selections used biotinylated HSA.

2) Trypsin selections against HSA:

10 In order to select dAbs with increased protease resistance compared to the parental clone and with potentially improved biophysical properties, trypsin was used in phage selections (see WO2008149143). Four rounds of selection were preformed against HSA. The first round of selection of error prone libraries was performed against passively coated HSA at 1mg/ml without trypsin; the second round against
15 passively coated HSA at 1mg/ml with 20µg/ml trypsin for 1hour at 37°C; the third round selection was performed by soluble selection using biotinylated HSA against 100 nM HSA with 20 µg/ml or 100 µg/ml trypsin for 1hour at 37°C. The final round of selection was performed by soluble selection using biotinylated HSA against 100nM HSA with 100 µg/ml trypsin overnight at 37°C.

20

3) Cross-over selections against HSA (round 1) and RSA (rounds 2-4):

The first round selection was carried out against 1mg/ml passively coated HSA or 1 µM HSA (soluble selection), followed by a further three rounds of soluble selections against biotinylated RSA at concentrations of 1 µM for round 1, 100nm
25 for round 2 and 20nM, 10nM or 1nM for round 3.

Screening strategy and affinity determination:

30

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- In each case after selection a pool of phage DNA from the appropriate round of selection is prepared using a QIAfilter* midiprep kit (Qiagen), the DNA is digested using the restriction enzymes SalI and NotI and the enriched V genes are ligated into the corresponding sites in pDOM5 the soluble expression vector which expresses the dAb with a myc tag (see PCT/EP2008/067789). The ligated DNA is used to electro-transform *E. coli* HB 2151 cells which are then grown overnight on agar plates containing the antibiotic carbenicillin. The resulting colonies are individually assessed for antigen binding. In each case at least 96 clones were tested for binding to HSA, CSA (*Cynomolgus* monkey Serum Albumin), MSA (mouse serum albumin) and RSA by BIAcore™ (surface plasmon resonance). MSA antigen was obtained from Sigma (essentially fatty acid free, ~99% (agarose gel electrophoresis), lyophilized powder Cat. No. A3559) and CSA was purified from *Cynomolgus* serum albumin using prometic blue resin (Amersham). Soluble dAb fragments were produced in bacterial culture in ONEX culture media (Novagen) overnight at 37°C in 96 well plates. The culture supernatant containing soluble dAb was centrifuged and analysed by BIAcore for binding to high density HSA, CSA, MSA and RSA CM5 chips. Clones were found to bind to all these species of serum albumin by off-rate screening. The clones were sequenced revealing unique dAb sequences.
- 20 The minimum identity to parent (at the amino acid level) of the clones selected was 97.2% (DOM7h-11-3: 97.2%, DOM7h-11-12: 98.2%, DOM7h-11-15: 96.3%, DOM7h-11-18: 98.2%, DOM7h-11-19: 97.2%)

- The minimum identity to parent (at the amino acid level) of the clones selected was 96.3% (DOM7h-14-10: 96.3%, DOM7h-14-18: 96.3%, DOM7h-14-19: 98.2%, DOM7h-14-28: 99.1%, DOM7h-14-36: 97.2%)

- Unique dAbs were expressed as bacterial supernatants in 2.5L shake flasks in Onex media at 30°C for 48hrs at 250rpm. dAbs were purified from the culture media by absorption to protein L agarose followed by elution with 10mM glycine pH2.0. Binding

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to HSA, CSA, MSA and RSA by BIAcore was confirmed using purified protein at 3 concentrations 1 μ M, 500nM and 50nM. To determine the binding affinity (K_D) of the AlbuAbs to each serum albumin; purified dAbs were analysed by BIAcore over albumin concentration range from 5000nM to 39nM (5000nM, 2500nM, 1250nM, 5 625nM, 312nM, 156nM, 78nM, 39nM).

Table 6

AlbuAb	Affinity (K_D) to SA (nM)	Kd	Ka
	Rat		
DOM7h-14	60	2.095E-01	4.00E+06
DOM7h-14-10	4	9.640E-03	4.57E+06
DOM7h-14-18	410	2.275E-01	5.60E+05
DOM 7h-14-19	890	2.870E-01	3.20E+05
DOM 7h-14-28	45 (140)	7.0E-02 (1.141e-1)	2.10E+06 (8.3e5)
DOM 7h-14-36	30 (6120)	2.9E-02 (5.54e-2)	1.55E+06 (9e3)
DOM 7h-11	2100	1.00E-01	4.80E+04
DOM 7h-11-3	10000 (88000)	(7.18e-1)	(8.11e3)
DOM 7h-11-12	200	5.22E-01	2.76E+06
DOM 7h-11-15	20	2.10E-02	1.10E+06
DOM 7h-11-18	80 (29000)	6.0E-02 (3.7e-1)	1.64E+06 (1.3e4)
DOM 7h-11-19	28 (17000)	9.1e-02	9.80E+05

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		(1.4e-1)	(8.1e3)
	Cyno		
DOM 7h-14	66	9.65E-02	1.50E+06
DOM 7h-14-10	9	1.15E-02	1.60E+06
DOM 7h-14-18	180	1.05E-01	6.30E+5
DOM 7h-14-19	225	1.56E-01	7.00E+05
DOM 7h-14-28	66 (136)	1.3E-01 (1.34e-1)	2.50E+06 (9.8e5)
DOM 7h-14-36	35 (7830)	1.9E-02 (1.1e-1)	9.80E+06 (1.43e4)
DOM 7h-11	1000	6.82E-01	8.00E+05
DOM 7h-11-3	670 (200)	9.6E-02 (1.5e-1)	2.90E+05 (7.26e5)
DOM 7h-11-12	≥6000		
DOM 7h-11-15	3	5.57E-03	5.80E+06
DOM 7h-11-18	10000 (65000)	1.36 (4.8e- 1)	2.25E+05 (7.3e3)
DOM 7h-11-19	≥10000 (375000)	(6.2e-1)	(1.7e3)
	Mouse		
DOM 7h-14	12	4.82E-02	4.10E+06
DOM 7h-14-10	30	3.41E-02	1.29E+06
DOM 7h-14-18	65	9.24E-02	2.28E+06
DOM 7h-14-19	60	5.76E-02	1.16E+06
DOM 7h-14-28	26 (31)	3.4E-02 (7.15e-2)	1.60E+06 (2.28e6)

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DOM 7h-14-36	35 (33)	2.3E-02 (7.06e-2)	8.70E+05 (2.11e6)
DOM 7h-11	5000	9.00E-01	
DOM 7h-11-3	≥10000 (36000)	(6.12e-1)	(1.67e4)
DOM 7h-11-12	130	1.89E-01	1.53E+06
DOM 7h-11-15	10	9.40E-03	1.10E+06
DOM 7h-11-18	150 (1600)	2.4E-02 (6.23e-2)	4.40E+05 (4e4)
DOM 7h-11-19	100 (18000)	3.7E-02 (8.8e-2)	1.40E+06 (4.9e3)
	Human		
DOM 7h-14	33	4.17E-02	1.43E+06
DOM 7h-14-10	12	1.39E-02	1.50E+06
DOM 7h-14-18	280	3.39E-02	1.89E+05
DOM 7h-14-19	70	5.25E-02	8.26E+05
DOM 7h-14-28	30 (8260)	3.3E-02 (5.6e-2)	1.24E+06 (6.78e3)
DOM 7h-14-36	28 (1260)	2.4E-02 (6.7e-2)	1.23E+06 (5.4e4)
DOM 7h-11	2800	6.41E-01	7.00E+05
DOM 7h-11-3	32 (130)	1.6E-02 (2.35e-2)	6.50E+05 (1.86e5)
DOM 7h-11-12	350	4.13E-01	1.26E+06
DOM 7h-11-15	1	1.84E-03	2.00E+06
DOM 7h-11-18	36 (32000)	5.1E-02	3.40E+06

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		(2.7e-1)	(8.39e3)
DOM 7h-11-19	65 (38000)	1.1E-01 (2.09e-1)	1.80E+06 (5.4e3)

*: values in brackets were derived from a second, independent SPR experiment.

All DOM7h-14 derived variants are cross-reactive to mouse, rat, human and cyno serum albumin. DOM7h-14-10 has improved affinity to rat, cyno and human serum albumin compared to parent. DOM7h-14-28 has an improved affinity to RSA. DOM7h-14-36 has an improved affinity to RSA, CSA and MSA.

DOM7h-11-3 has improved affinity to CSA and HSA. DOM7h-11-12 has improved affinity to RSA, MSA and HSA. DOM7h-11-15 has improved affinity to RSA, MSA, CSA and HSA. DOM7h-11-18 and DOM7h-11-19 have improved affinity to RSA, MSA and HSA.

Example 3: Origins of key DOM7h-11 lineage clones:

DOM7h-11-3: From affinity maturation performed against HSA using the CDR2 library (Y49, A50, A51, S53), round 3 output 10nM HSA

DOM7h-11-12: From affinity maturation performed against HSA using the error prone library, round 3 outputs (100nM, HSA) with 100ug/ml trypsin.

DOM7h-11-15: From cross-over selections performed against HSA as round 1 followed by additional 3 rounds of selections against RSA using the CDR2 library (Y49, A50, A51, S53) at round 3 selection with 1nM of RSA.

DOM7h-11-18 From cross-over selections performed against HSA as round 1 followed by additional 3 rounds of selections against RSA using the error prone library, round 3 output at 20nM of RSA

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DOM7h-11-19 From cross-over selections performed against HSA as round 1 followed by additional 3 rounds of selections against RSA using the error prone library, round 3 output at 5nM of RSA

5

Table 7: CDR sequences (according to Kabat; ref. as above)

AlbudAb	CDR		
	CDR1	CDR2	CDR3
DPK9 Vk dummy	SQSISSYLN (SEQ ID NO: 335)	YAASSLQS (SEQ ID NO: 336)	QQSYSTPNT (SEQ ID NO: 337)
DOM7h-11	SRPIGTTLS (SEQ ID NO: 338)	WFGSRLQS (SEQ ID NO: 339)	AQAGTHPTT (SEQ ID NO: 340)
DOM7h-11-12	SRPIGTMLS (SEQ ID NO: 341)	LFGSRLQS (SEQ ID NO: 342)	AQAGTHPTT (SEQ ID NO: 343)
DOM 7h-11-15	SRPIGTMLS (SEQ ID NO: 344)	LAFSRLQS (SEQ ID NO: 345)	AQAGTHPTT (SEQ ID NO: 346)
DOM 7h-11-18	SRPIGTMLS (SEQ ID NO: 347)	WFGSRLQS (SEQ ID NO: 348)	AQAGTHPTT (SEQ ID NO: 349)
DOM 7h-11-19	SRPIGTMLS (SEQ ID NO: 350)	LFGSRLQS (SEQ ID NO: 351)	AQTGTHPTT (SEQ ID NO: 352)
DOM 7h-11-3	SRPIGTTLS (SEQ ID NO: 353)	LWFSRLQS (SEQ ID NO: 354)	AQAGTHPTT (SEQ ID NO: 355)

10 **Example 4: Origins of key DOM7h-14 lineage clones:**

DOM7h-14-19: From affinity maturation performed against HSA using the error prone library, round 3 outputs (100nM, HSA) with 100ug/ml trypsin.

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DOM7h-14-10, DOM7h-14-18, DOM7h-14-28, DOM7h-14-36: From affinity maturation performed against HSA using CDR3 library (Y92, Y93, T94, N96), round 3 output.

5 **Table 8: CDR sequences (according to Kabat; ref. as above)**

AlbudAb	CDR		
	CDR1	CDR2	CDR3
DPK9 Vk dummy	SQSISSYLN (SEQ ID NO: 335)	YAASSLQS (SEQ ID NO: 336)	QQSYSTPNT (SEQ ID NO: 337)
DOM 7h-14	SQWIGSQLS (SEQ ID NO: 356)	MWRSSLQS (SEQ ID NO: 357)	AQGAALPRT (SEQ ID NO: 358)
DOM 7h-14-10	SQWIGSQLS (SEQ ID NO: 359)	MWRSSLQS (SEQ ID NO: 360)	AQGLRHPKT (SEQ ID NO: 361)
DOM 7h-14-18	SQWIGSQLS (SEQ ID NO: 362)	MWRSSLQS (SEQ ID NO: 363)	AQGLMKPMT (SEQ ID NO: 364)
DOM 7h-14-19	SQWIGSQLS (SEQ ID NO: 365)	MWRSSLQS (SEQ ID NO: 366)	AQGAALPRT (SEQ ID NO: 367)
DOM 7h-14-28	SQWIGSQLS (SEQ ID NO: 368)	MWRSSLQS (SEQ ID NO: 369)	AQGAALPKT (SEQ ID NO: 370)
DOM 7h-14-36	SQWIGSQLS (SEQ ID NO: 371)	MWRSSLQS (SEQ ID NO: 372)	AQGFKKPRT (SEQ ID NO: 373)

Example 5: Expression and Biophysical Characterisation:

- 10 The routine bacterial expression level in 2.5L shake flasks was determined following culture in Onex media at 30°C for 48hrs at 250rpm. The biophysical characteristics were determined by SEC MALLS and DSC.
- SEC MALLS (size exclusion chromatography with multi-angle-LASER-light-scattering) is a non-invasive technique for the characterizing of macromolecules in

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solution. Briefly, proteins (at concentration of 1mg/mL in buffer Dulbecco's PBS at 0.5 ml/min are separated according to their hydrodynamic properties by size exclusion chromatography (column: TSK3000 from TOSOH Biosciences; S200 from Pharmacia). Following separation, the propensity of the protein to scatter light is measured using a multi-angle-LASER-light-scattering (MALLS) detector. The intensity of the scattered light while protein passes through the detector is measured as a function of angle. This measurement taken together with the protein concentration determined using the refractive index (RI) detector allows calculation of the molar mass using appropriate equations (integral part of the analysis software Astra v.5.3.4.12).

- 10 DSC (Differential Scanning Calorimetry): briefly, the protein is heated at a constant rate of 180 °C/hrs (at 1mg/mL in PBS) and a detectable heat change associated with thermal denaturation measured. The transition midpoint (T_m) is determined, which is described as the temperature where 50% of the protein is in its native conformation and the other 50% is denatured. Here, DSC determined the apparent transition midpoint
- 15 (T_m) as most of the proteins examined do not fully refold. The higher the T_m , the more stable the molecule. Unfolding curves were analysed by non-2-state equations. The software package used was Origin^R v7.0383.

20 **Table 9**

AlbudAb	Biophysical parameters	
	SEC MALLS	DSC T_m (°C)
DOM7h-14	M	60
DOM 7h-14-10	M	59
DOM 7h-14-18	M	58
DOM 7h-14-19	M	59
DOM 7h-14-28	M	58.3/60.2
DOM 7h-14-36	M	59.2

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DOM 7h-11	M	66.9-72.2
DOM 7h-11-3	M (95%)*	66.6/70.5
DOM 7h-11-12	M (<2%D)	71.7
DOM 7h-11-15	M (<5%D)	58.5-60.5
DOM 7h-11-18	M (98%)	58.9/65.8
DOM 7h-11-19	M	71.8/76.6

* in one other trial, monomer was primarily seen by SEC MALLS, although lower than 95%

We observed expression levels for all clones in Table 9 in the range from 15 to 119mg/L in *E coli*.

5

For DOM7h-14 and DOM7h-11 variants, favorable biophysical parameters (monomeric in solution as determined by SEC MALLs and appT_m of >55°C as determined by DSC) and expression levels were maintained during affinity maturation. Monomeric state is advantageous because it avoids dimerisation and the risk of products that may cross-link targets such as cell-surface receptors.

10

Example 6: Determination of serum half life in rat, mouse and *Cynomolgus* monkey

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AlbudAbs DOM7h-14-10, DOM7h-14-18, DOM7h-14-19, DOM7h-11, DOM7h11-12 and DOM7h-11-15 were cloned into the pDOM5 vector. For each AlbudAbTM, 20-50mg quantities were expressed in *E. coli* and purified from bacterial culture supernatant using protein L affinity resin and eluted with 100mM glycine pH2. The proteins were concentrated to greater than 1mg/ml, buffer exchanged into PBS and endotoxin depleted using Q spin* columns (Vivascience). For Rat pharmacokinetic (PK) analysis, AlbudAbs were dosed as single i.v injections at 2.5mg/kg using 3 rats per

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compound. Serum samples were taken at 0.16, 1, 4, 12, 24, 48, 72, 120, 168hrs.

Analysis of serum levels was by anti-myc ELISA as per the method described below.

For Mouse PK, DOM7h-11, DOM7h11-12 and DOM7h-11-15 were dosed as single i.v
 5 injections at 2.5mg/kg per dose group of 3 subjects and serum samples taken at 10mins;
 1h; 8h; 24h; 48h; 72h; 96h. Analysis of serum levels was by anti-myc ELISA as per the
 method described below.

For *Cynomolgus* monkey PK DOM7h-14-10 and DOM7h-11-15 were dosed as single
 10 i.v injections at 2.5mg/kg into 3 female *Cynomolgus* monkeys per dose group and
 serum samples taken at 0.083, 0.25, 0.5, 1, 2, 4, 8, 24, 48, 96, 144, 192, 288, 336,
 504hrs. Analysis of serum levels was by anti-myc ELISA as per the method described
 below.

15 Anti-myc ELISA method

The AlbuAb concentration in serum was measured by anti- myc ELISA. Briefly, goat
 anti- myc polyclonal antibody (1:500; Abcam, catalogue number ab9132) was coated
 overnight onto Nunc 96-well Maxisorp* plates and blocked with 5% BSA/PBS + 1%
 tween. Serum samples were added at a range of dilutions alongside a standard at known
 20 concentrations. Bound myc-tagged AlbuAb was then detected using a rabbit
 polyclonal anti-Vk (1:1000; in-house reagent, bleeds were pooled and protein A
 purified before use) followed by an anti-rabbit IgG HRP antibody (1:10,000; Sigma,
 catalogue number A2074). Plates were washed between each stage of the assay with 3 x
 PBS+0.1% Tween20* followed by 3 x PBS. TMB (SureBlue* TMB 1-Component
 25 Microwell Peroxidase Substrate, KPL, catalogue number 52-00-00) was added after the
 last wash and was allowed to develop. This was stopped with 1M HCl and the signal
 was then measured using absorbance at 450nm.

From the raw ELISA data, the concentration of unknown samples was established by
 30 interpolation against the standard curve taking into account dilution factors. The mean

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- concentration result from each time point was determined from replicate values and entered into WinNonLin analysis package (eg version 5.1 (available from Pharsight Corp., Mountain View, CA94040, USA). The data was fitted using a non-compartmental model, where PK parameters were estimated by the software to give
- 5 terminal half-lives. Dosing information and time points were selected to reflect the terminal phase of each PK profile.

Table 10: Single AlbudAb™ PK

Species	AlbudAb	Albumin K _D (nM)	PK parameters			
			AUC h x µg/ml	CL ml/h/kg	t _{1/2} h	V _z ml/kg
Rat	DOM7h-14*	60				
	DOM7h-14-10	4	2134.6	1.2	42.1	71.2
	DOM7h-14-18	410	617.3	4.1	38.4	228.1
	DOM 7h-14-19	890	632.6	4.1	36.3	213.3
	DOM 7h-11	2100	320.1	7.8	23.3	263.9
	DOM 7h-11-12	200	398.7	6.4	35.5	321.2
	DOM 7h-11-15	20	843.4	3.0	30.3	130.7
mouse	DOM 7h-11	5000	304.7	8.2	18.3	216.8
	DOM 7h-11-12	130	646.6	3.9	43.9	244.8
	DOM 7h-11-15	10	499.2	5.0	33.7	243.4
Cyno	DOM 7h-14*	66			217.5	
	DOM 7h-14-10	9	6174.6	0.4	200.8	117.8

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	DOM 7h-11*	3300			135.1	
	DOM 7h-11-15	3	4195	0.6	198.1	170.3

* Historical data

Pharmacokinetic parameters derived from rat, mouse and cynomolgus monkey studies were fitted using a non-compartmental model. Key: AUC: Area under the curve from dosing time extrapolated to infinity; CL: clearance; t_{1/2}: is the time during which the blood concentration is halved; Vz: volume of distribution based on the terminal phase.

DOM7h-11 12 and DOM7h-11-15 have an improved AUC and t_{1/2} in rat and mouse compared to parent. DOM7h-11-15 also has an improved AUC and t_{1/2} in cyno compared to parent. This improvement in AUC/t_{1/2} correlates with an improved in vitro KD to serum albumin.

15 **Example 7: AlbudAbTM IFN fusions**

Cloning and expression

As well as single AlbudAbs, the affinity matured Vk Albudabs were linked to Interferon alpha 2b (IFN α 2b) to determine whether a useful PK of the AlbudAb was maintained as a fusion protein.

Interferon alpha 2b amino acid sequence:

CDLPQTHSLGSRRTLMLLAQMRRISLFSCLKDRHDFGFPQEEFGNQFQKAETIP
VLHEMIQQIFNLFSTKDSSAAWDETLLDKFYTELYQQLNDLEACVIQGVGVGTET
25 PLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSLSTNLQESLRS
KE (SEQ ID NO:374)

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Interferon alpha 2b nucleotide sequence:

TGTGATCTGCCTCAAACCCACAGCCTGGGTAGCAGGAGGACCTTGATGCTC
 CTGGCACAGATGAGGAGAATCTCTCTTTTCTCCTGCTTGAAGGACAGACATG
 ACTTTGGATTTCCCCAGGAGGAGTTTGGCAACCAGTTCCAAAAGGCTGAAA
 5 CCATCCCTGTCCTCCATGAGATGATCCAGCAGATCTTCAATCTCTTCAGCAC
 AAAGGACTCATCTGCTGCTTGGGATGAGACCCTCCTAGACAAATTCTACACT
 GAACTCTACCAGCAGCTGAATGACCTGGAAGCCTGTGTGATACAGGGGGTG
 GGGGTGACAGAGACTCCCCTGATGAAGGAGGACTCCATTCTGGCTGTGAGG
 AAATACTTCCAAAGAATCACTCTCTATCTGAAAGAGAAGAAATACAGCCCT
 10 TGTGCCTGGGAGGTTGTCAGAGCAGAAATCATGAGATCTTTTTCTTTGTCAA
 CAAACTTGCAAGAAAGTTTAAGAAGTAAGGAA (SEQ ID NO:375)

IFN α 2b was linked to the AlbudAb via a TVAAPS linker region (see WO2007085814).
 The constructs were cloned by SOE-PCR (single overlap extension according to the
 15 method of Horton *et al.* Gene, 77, p61 (1989)). PCR amplification of the AlbudAb and
 IFN sequences were carried out separately using primers with a ~15 base pair overlap at
 the TVAAPS linker region. The primers used are as follows:-

IFN α 2b SOE fragment 5'	GCCCGGATCCACCGGCTGTGATCTG (SEQ ID NO:376)
IFN α 2b SOE fragment 3'	GGAGGATGGAGACTGGGTCATCTGGATGTC (SEQ ID NO:377)
Vk SOE fragment 5'	GACATCCAGATGACCCAGTCTCCATCCTCC (SEQ ID NO:378)
Vk SOE fragment 3' to also introduce a myc tag	GCGCAAGCTTTTATTAATTCAGATCCTCTTC TGAGATGAGTTTTTGTCTGCGGCCGCCCCGT TTGATTTCCACCTTGGTCCC (SEQ ID NO:379)

20

The fragments were purified separately and subsequently assembled in a SOE (single overlap extension PCR extension) reaction using only the flanking primers.

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IFN α 2b SOE fragment 5' GCCCGGATCCACCGGCTGTGATCTG (SEQ ID NO:380)
 GCGCAAGCTTTTATTAATTCAGATCCTCTTC
 Vk SOE fragment 3' to TGAGATGAGTTTTTGTCTGCGGCCGCCCCGT
 also introduce a myc tag TTGATTTCACCTTGGTCCC (SEQ ID NO:381)

The assembled PCR product was digested using the restriction enzymes BamHI and HindIII and the gene ligated into the corresponding sites in the pDOM50, a mammalian
 5 expression vector which is a pTT5 derivative with an N-terminal V-J2-C mouse IgG secretory leader sequence to facilitate expression into the cell media.

Leader sequence (amino acid):

METDTLLLWVLLLWVPGSTG (SEQ ID NO:382)

10

Leader sequence (nucleotide):

ATGGAGACCGACACCCTGCTGCTGTGGGTGCTGCTGCTGTGGGTGCCCCGGA
 TCCACCGGGC (SEQ ID NO:383)

15

Plasmid DNA was prepared using QIAfilter megaprep (Qiagen). 1 μ g DNA/ml was transfected with 293-Fectin into HEK293E cells and grown in serum free media. The protein is expressed in culture for 5 days and purified from culture supernatant using protein L affinity resin and eluted with 100mM glycine pH2. The proteins were
 20 concentrated to greater than 1mg/ml, buffer exchanged into PBS and endotoxin depleted using Q spin columns (Vivascience).

Table 11: Interferon alpha 2b-AlbudAb sequences with and without myc-tag (as amino acid- and nucleotide sequence)

25

The Interferon alpha 2b is N-terminal to the AlbudAb in the following fusions.

	aa + myc	nt + myc	aa no tag	nt no tag
DMS7321 (IFN α 2b- DOM7h- 14)	CDLPQTHSLGSRRT LMLLAQMRRISLFS CLKDRHDFGFPQE EFGNQFQKAETIPV LHEMIQQIFNLFST KDSSAAWDETLLD KFYTELYQQNLNDL EACVIQGVGVTTETP LMKEDSILAVRKY FQRITLYLKEKKYS PCAWEVVRAEIMR SFSLSSTNLQESLRS KETVAAPSDIQMT QSPSSLSASVGDRV TITCRASQWIGSQL SWYQQKPGKAPKL LIMWRSSLQSGVPS RFSGSGSGTDFTLT ISSLQPEDFATYYC AQGAALPRTFGQG TKVEIKR AAAEQKLISEEDL N* (SEQ ID NO:384)	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTTTC TTTGTCTCTCTT GTCTAAAGGAC CGTCACGACTT CGGATTCCCTC AGGAAGAGTTT GGAAACCAATT CCAAAAAGCA GAAACTATTCC TGTCTTGCACG AAATGATCCAG CAAATATTCAA TTTGTTTTCTA CAAAGGACTC ATCAGCCGCTT GGGATGAAAC TCTGTTAGATA AATTCTACACT GAACTATATCA ACAACTGAAC GATCTAGAGGC TTGCGTTATTC	CDLPQTHSLG SRRTLMLLA QMRRISLFSC LKDRHDFGFP QEEFGNQFQ KAETIPVLHE MIQQIFNLF TKDSSAAWD ETLLDKFYTE LYQQNLNDLE ACVIQGVGV TETPLMKEDS ILAVRKYFQR ITLYLKEKKY SPCAWEVVR AEIMRSFSL TNLQESLSK ETVAAPSDIQ MTQSPSSLSA SVGDRVITC RASQWIGSQL SWYQQKPGK APKLLIMWR SSLQSGVPSR FSGSGSGTDF TLTISSLQPED FATYYCAQG AALPRTFGQ	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTTTC TTTGTCTCTCTT GTCTAAAGGA CCGTCACGACT TCGGATTCCCT CAGGAAGAGT TTGGAAACCA ATTCCAAAA GCAGAACTA TTCCTGTCTTG CACGAAATGA TCCAGCAAATA TTCAATTTGTT TTCTACAAAGG ACTCATCAGCC GCTTGGGATGA AACTCTGTTAG ATAAATTCTAC ACTGAACTATA TCAACAACCTGA ACGATCTAGA GGCTTGCGTTA

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		AGGGTGTAGG AGTTACTGAAA CTCCCCTAATG AAAGAAGATT CAATTCTAGCC GTTAGAAAATA CTTTCAGCGTA TCACATTGTAT TTAAAGGAAA AGAAATACTCC CCATGTGCATG GGAGGTGGTTA GAGCAGAAAT TATGAGGTCCT TCTCTCTTCT ACGAATTTGCA AGAATCTTTGA GATCTAAGGA AACCGTCGCTG CTCCATCTGAC ATCCAGATGAC CCAGTCTCCAT CCTCCCTGTCT GCATCTGTAGG AGACCGTGTCA CCATCACTTGC CGGGCAAGTC AGTGGATTGGG TCTCAGTTATC TTGGTACCAGC	GTKVEIKR (SEQ ID NO:386)	TTCAGGGTGTA GGAGTTACTGA AACTCCCCTAA TGAAAGAAGA TTCAATTCTAG CCGTTAGAAA ATACTTTCAGC GTATCACATTG TATTTAAAGGA AAAGAAATAC TCCCCATGTGC ATGGGAGGTG GTTAGAGCAG AAATTATGAG GTCCTTCTCTC TTTCTACGAAT TTGCAAGAATC TTTGAGATCTA AGGAAACCGT CGCTGCTCCAT CTGACATCCAG ATGACCCAGTC TCCATCCTCCC TGTCTGCATCT GTAGGAGACC GTGTCACCATC ACTTGCCGGGC AAGTCAGTGG ATTGGGTCTCA GTTATCTTGGT
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		AGAAACCAGG GAAAGCCCCTA AGCTCCTGATC ATGTGGCGTTC CTCGTTGCAAA GTGGGGTCCCA TCACGTTTCAG TGGCAGTGGAT CTGGGACAGAT TTCACCTCTCAC CATCAGCAGTC TGCAACCTGAA GATTTTGCTAC GTACTACTGTG CTCAGGGTGCG GCGTTGCCTAG GACGTTTCGGCC AAGGGACCAA GGTGGAATC AAACGGG GCGG CCGCAGAACA AAA ACTCATC TCAGAAGAGG ATCTGAATTA A (SEQ ID NO:385)		ACCAGCAGAA ACCAGGGAAA GCCCCTAAGCT CCTGATCATGT GGCGTTCCTCG TTGCAAAGTGG GGTCCCATCAC GTTTCAGTGGC AGTGGATCTGG GACAGATTTCA CTCTCACCATC AGCAGTCTGCA ACCTGAAGATT TTGCTACGTAC TACTGTGCTCA GGGTGCGGCG TTGCCTAGGAC GTTCGGCCAAG GGACCAAGGT GGAAATCAAA CGG (SEQ ID NO:387)
DMS732 (IFN α 2b- DOM7h- 14-10)	CDLPQTHSLGSRRT LMLLAQMRRISLFS CLKDRHDFGFPQE EFGNQFQKAETIPV	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA	CDLPQTHSLG SRRTLMLLA QMRRISLFSC LKDRHDFGFP	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA

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LHEMIQQIFNLFST	TTGATGTTATT	QEEFGNQFQ	TTGATGTTATT
KDSSAAWDETLLD	AGCACAAATG	KAETIPVLHE	AGCACAAATG
KFYTELYQQNLNDL	CGTAGAATTTTC	MIQQIFNLFS	CGTAGAATTTTC
EACVIQGVGVGTETP	TTTGTTCTCTT	TKDSSAAWD	TTTGTTCTCTT
LMKEDSILAVRKY	GTCTAAAGGAC	ETLLDKFYTE	GTCTAAAGGA
FQRITLYLKEKKYS	CGTCACGACTT	LYQQNLNDLE	CCGTCACGACT
PCAWEVVRAEIMR	CGGATTCCCTC	ACVIQGVGV	TCGGATTCCCT
SFSLSTNLQESLRS	AGGAAGAGTTT	TETPLMKEDS	CAGGAAGAGT
KETVAAPSDIQMT	GGAAACCAATT	ILAVRKYFQR	TTGGAAACCA
QSPSSLASVGDV	CCAAAAAGCA	ITLYLKEKKY	ATTCCAAAAA
TITCRASQWIGSQL	GAAACTATTCC	SPCAWEVVR	GCAGAAACTA
SWYQQKPGKAPKL	TGTCTTGCACG	AEIMRSFSL	TTCCTGTCTTG
LIMWRSSLQSGVPS	AAATGATCCAG	TNLQESLSK	CACGAAATGA
RFSGSGSGTDFTLT	CAAATATTCAA	ETVAAPSDIQ	TCCAGCAAATA
ISSLQPEDFATYYC	TTTGTTTTCTA	MTQSPSSL	TTCAATTTGTT
AQGLRHPKTFGQG	CAAAGGACTC	SVGDRVTITC	TTCTACAAAGG
TKVEIKR	ATCAGCCGCTT	RASQWIGSQL	ACTCATCAGCC
AAAEQKLISEEDL	GGGATGAAAC	SWYQQKPGK	GCTTGGGATGA
N* (SEQ ID NO:388)	TCTGTAGATA	APKLLIMWR	AACTCTGTTAG
	AATTCTACACT	SSLQSGVPSR	ATAAATTCTAC
	GAACTATATCA	FSGSGSGTDF	ACTGAACTATA
	ACAACTGAAC	TLTISSLQPED	TCAACAACTGA
	GATCTAGAGGC	FATYYCAQG	ACGATCTAGA
	TTGCGTTATTC	LRHPKTFGQ	GGCTTGCGTTA
	AGGGTGTAGG	GTKVEIKR	TTCAGGGTGTA
	AGTTACTGAAA	(SEQ ID	GGAGTTACTGA
	CTCCCCTAATG	NO:390)	AACTCCCCTAA
	AAAGAAGATT		TGAAAGAAGA
	CAATTCTAGCC		TTCAATTCTAG
	GTTAGAAAATA		CCGTTAGAAA

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	CTTTCAGCGTA TCACATTGTAT TTAAAGGAAA AGAAATACTCC CCATGTGCATG GGAGGTGGTTA GAGCAGAAAT TATGAGGTCCT TCTCTCTTTCT ACGAATTTGCA AGAATCTTTGA GATCTAAGGA AACCGTCGCTG CTCCATCTGAC ATCCAGATGAC CCAGTCTCCAT CCTCCCTGTCT GCATCTGTAGG AGACCGTGTCA CCATCACTTGC CGGGCAAGTC AGTGGATTGGG TCTCAGTTATC TTGGTACCAGC AGAAACCAGG GAAAGCCCCTA AGCTCCTGATC ATGTGGCGTTC CTCGTTGCAAA GTGGGGTCCCA		ATACTTTCAGC GTATCACATTG TATTTAAAGGA AAAGAAATAC TCCCCATGTGC ATGGGAGGTG GTTAGAGCAG AAATTATGAG GTCCTTCTCTC TTTCTACGAAT TTGCAAGAATC TTTGAGATCTA AGGAAACCGT CGCTGCTCCAT CTGACATCCAG ATGACCCAGTC TCCATCCTCCC TGTCTGCATCT GTAGGAGACC GTGTCACCATC ACTTGCCGGGC AAGTCAGTGG ATTGGGTCTCA GTTATCTTGGT ACCAGCAGAA ACCAGGGAAA GCCCCTAAGCT CCTGATCATGT GGCGTTCCTCG TTGCAAAGTGG
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		TCACGTTTCAG TGGCAGTGGAT CTGGGACAGAT TTCACTCTCAC CATCAGCAGTC TGCAACCTGAA GATTTTGCTAC GTACTACTGTG CTCAGGGTTTG AGGCATCCTAA GACGTTCGGCC AAGGGACCAA GGTGGAAATC AAACGGG CGG CCGCAGAACA AAA ACTCATC TCAGAAGAGG ATCTGAATTA A (SEQ ID NO:389)		GGTCCCATCAC GTTTCAGTGGC AGTGGATCTGG GACAGATTTCA CTCTCACCATC AGCAGTCTGCA ACCTGAAGATT TTGCTACGTAC TACTGTGCTCA GGGTTTGAGGC ATCCTAAGACG TTCGGCCAAGG GACCAAGGTG GAAATCAAAC GG (SEQ ID NO:391)
DMS7323 (IFN α 2b- DOM7h- 14-18)	CDLPQTHSLGSRRT LMLLAQMRRISLFS CLKDRHDFGFPQE EFGNQFQKAETIPV LHEMIQQIFNLFST KDSSAAWDETLLD KFYTELYQQLNDL EACVIQGVGVETETP LMKEDSILAVRKY FQRITLYLKEKKYS	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTC TTTGTTCTCTT GTCTAAAGGAC CGTCACGACTT	CDLPQTHSLG SRRTLMLLA QMRRISLFSC LKDRHDFGFP QEEFGNQFQ KAETIPVLHE MIQQIFNLF TKDSSAAWD ETLLDKFYTE LYQQLNDLE	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTC TTTGTTCTCTT GTCTAAAGGA CCGTCACGACT

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PCAWEVVRAEIMR	CGGATTCCCTC	ACVIQGVGV	TCGGATTCCCT
SFSLSTNLQESLRS	AGGAAGAGTTT	TETPLMKEDS	CAGGAAGAGT
KETVAAPSDIQMT	GGAAACCAATT	ILAVRKYFQR	TTGGAAACCA
QSPSSLSASVGDRV	CCAAAAAGCA	ITLYLKEKKY	ATTCCAAAAA
TITCRASQWIGSQL	GAAACTATTCC	SPCAWEVVR	GCAGAAACTA
SWYQQKPGKAPKL	TGTCTTGCACG	AEIMRSFSL	TTCCTGTCTTG
LIMWRSSLQSGVPS	AAATGATCCAG	TNLQESLSK	CACGAAATGA
RFSGSGSGTDFTLT	CAAATATTCAA	ETVAAPSDIQ	TCCAGCAAATA
ISSLQPEDFATYYC	TTTGTTTTCTA	MTQSPSSLSA	TTCAATTTGTT
AQGLMKPMTFGQ	CAAAGGACTC	SVGDRVITIC	TTCTACAAAGG
GTKVEIKRAAAEQ	ATCAGCCGCTT	RASQWIGSQL	ACTCATCAGCC
KLISEEDLN* (SEQ	GGGATGAAAC	SWYQQKPGK	GCTTGGGATGA
ID NO:392)	TCTGTTAGATA	APKLLIMWR	AACTCTGTTAG
	AATTCTACACT	SSLQSGVPSR	ATAAATTCTAC
	GAACTATATCA	FSGSGSGTDF	ACTGAACTATA
	ACAACTGAAC	TLTISSLQPED	TCAACAACCTGA
	GATCTAGAGGC	FATYYCAQG	ACGATCTAGA
	TTGCGTTATTC	LMKPMTFGQ	GGCTTGCGTTA
	AGGGTGTAGG	GTKVEIKR	TTCAGGGTGTA
	AGTTACTGAAA	(SEQ ID	GGAGTTACTGA
	CTCCCCTAATG	NO:394)	AACTCCCCTAA
	AAAGAAGATT		TGAAAGAAGA
	CAATTCTAGCC		TTCAATTCTAG
	GTTAGAAAATA		CCGTTAGAAA
	CTTTCAGCGTA		ATACTTTCAGC
	TCACATTGTAT		GTATCACATTG
	TTAAAGGAAA		TATTTAAAGGA
	AGAAATACTCC		AAAGAAATAC
	CCATGTGCATG		TCCCCATGTGC
	GGAGGTGGTTA		ATGGGAGGTG

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		GAGCAGAAAT TATGAGGTCCT TCTCTCTTTCT ACGAATTTGCA AGAATCTTTGA GATCTAAGGA AACCGTCGCTG CTCCATCTGAC ATCCAGATGAC CCAGTCTCCAT CCTCCCTGTCT GCATCTGTAGG AGACCGTGTCA CCATCACTTGC CGGGCAAGTC AGTGGATTGGG TCTCAGTTATC TTGGTACCAGC AGAAACCAGG GAAAGCCCCTA AGCTCCTGATC ATGTGGCGTTC CTCGTTGCAAA GTGGGGTCCCA TCACGTTTCAG TGGCAGTGGAT CTGGGACAGAT TTCACCTCTCAC CATCAGCAGTC TGCAACCTGAA		GTTAGAGCAG AAATTATGAG GTCCTTCTCTC TTTCTACGAAT TTGCAAGAATC TTTGAGATCTA AGGAAACCGT CGCTGCTCCAT CTGACATCCAG ATGACCCAGTC TCCATCCTCCC TGTCTGCATCT GTAGGAGACC GTGTCACCATC ACTTGCCGGGC AAGTCAGTGG ATTGGGTCTCA GTTATCTTGGT ACCAGCAGAA ACCAGGGAAA GCCCCTAAGCT CCTGATCATGT GGCGTTCCTCG TTGCAAAGTGG GGTCCCATCAC GTTTCAGTGGC AGTGGATCTGG GACAGATTTCA CTCTCACCATC AGCAGTCTGCA
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		GATTTTGCTAC GTACTACTGTG CTCAGGGTCTT ATGAAGCCTAT GACGTTCGGCC AAGGGACCAA GGTGGAAATC AAACGGG CGG CCGCAGAACA AAA ACTCATC TCAGAAGAGG ATCTGAATTA A (SEQ ID NO:393)		ACCTGAAGATT TTGCTACGTAC TACTGTGCTCA GGGTCTTATGA AGCCTATGACG TTCGGCCAAGG GACCAAGGTG GAAATCAAAC GG (SEQ ID NO:395)
DMS7324 (IFN α 2b- DOM7h- 14-19)	CDLPQTHSLGSRRT LMLLAQMRRISLFS CLKDRHDFGFPQE EFGNQFQKAETIPV LHEMIQQIFNLFST KDSSAAWDETLDD KFYTELYQQLNDL EACVIQGVGVETETP LMKEDSILAVRKY FQRITLYLKEKKYS PCAWEVVRAEIMR SFSLSSTNLQESLRS KETVAAPSDIQMT QSPSSLSASVGDRV TISCRASQWIGSQL SWYQQKPGEAPKL	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTTTC TTTGTCTCTCTT GTCTAAAGGAC CGTCACGACTT CGGATTCCCTC AGGAAGAGTTT GGAAACCAATT CCAAAAAGCA GAAACTATTCC TGTCTTGCACG	CDLPQTHSLG SRRTLMLLA QMRRISLFSC LKDRHDFGFP QEFGNQFQ KAETIPVLHE MIQQIFNLFS TKDSSAAWD ETLLDKFYTE LYQQLNDLE ACVIQGVGV TETPLMKEDS ILAVRKYFQR ITLYLKEKKY SPCAWEVVR AEIMRSFSL	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTTTC TTTGTCTCTCTT GTCTAAAGGA CCGTCACGACT TCGGATTCCCT CAGGAAGAGT TTGGAAACCA ATTCCAAAAA GCAGAAACTA TTCCTGTCTTG

- 108 -

LIMWRSSLQSGVPS RFSGSGSGTDFTLT ISSLQPEDFATYYC AQGAALPRTFGQG TKVEIKR AAAEQKLISEEDL N* (SEQ ID NO:396)	AAATGATCCAG CAAATATTCAA TTTGTTTTCTA CAAAGGACTC ATCAGCCGCTT GGGATGAAAC TCTGTTAGATA AATTCTACACT GAACTATATCA ACAACTGAAC GATCTAGAGGC TTGCGTTATTC AGGGTGTAGG AGTTACTGAAA CTCCCCTAATG AAAGAAGATT CAATTCTAGCC GTTAGAAAATA CTTTCAGCGTA TCACATTGTAT TTAAAGGAAA AGAAATACTCC CCATGTGCATG GGAGGTGGTTA GAGCAGAAAT TATGAGGTCCT TCTCTCTTCT ACGAATTTGCA AGAATCTTTGA GATCTAAGGA	TNLQESLRSK ETVAAPSDIQ MTQSPSSLSA SVGDRVTISC RASQWIGSQL SWYQQKPGE APKLLIMWR SSLQSGVPSR FSGSGSGTDF TLTISSLQPED FATYYCAQG AALPRTFGQ GTKVEIKR (SEQ ID NO:398)	CACGAAATGA TCCAGCAAATA TTCAATTTGTT TTCTACAAAGG ACTCATCAGCC GCTTGGGATGA AACTCTGTTAG ATAAATTCTAC ACTGAACTATA TCAACAACCTGA ACGATCTAGA GGCTTGCGTTA TTCAGGGTGTA GGAGTTACTGA AACTCCCCTAA TGAAAGAAGA TTCAATTCTAG CCGTTAGAAA ATACTTTCAGC GTATCACATTG TATTTAAAGGA AAAGAAATAC TCCCCATGTGC ATGGGAGGTG GTTAGAGCAG AAATTATGAG GTCCTTCTCTC TTTCTACGAAT TTGCAAGAATC TTTGAGATCTA
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	AACCGTCGCTG CTCCATCTGAC ATCCAGATGAC CCAGTcTCCAT CCTCCCTGTCT GCATCTGTAGG AGACCGTGTCA CCATCTCTTGC CGGGCAAGTC AGTGGATTGGG TCTCAGTTATC TTGGTACCAGC AGAAACCAGG GGAAGCCCCTA AGCTCCTGATC ATGTGGCGTTC CTCGTTGCAAA GTGGGGTCCCA TCACGTTTCAG TGGCAGTGGAT CTGGGACAGAT TTCACTCTCAC CATCAGCAGTC TGCAACCTGAA GATTTTGCTAC GTACTACTGTG CTCAGGGTGCG GCGTTGCCTAG GACGTTGCGCC AAGGGACCAA		AGGAAACCGT CGCTGCTCCAT CTGACATCCAG ATGACCCAGTc TCCATCCTCCC TGTCTGCATCT GTAGGAGACC GTGTCACCATC TCTTGCCGGGC AAGTCAGTGG ATTGGGTCTCA GTTATCTTGGT ACCAGCAGAA ACCAGGGGAA GCCCCTAAGCT CCTGATCATGT GGCGTTCCTCG TTGCAAAGTGG GGTCCCATCAC GTTTCAGTGGC AGTGGATCTGG GACAGATTTCA CTCTCACCATC AGCAGTCTGCA ACCTGAAGATT TTGCTACGTAC TACTGTGCTCA GGGTGCGGCG TTGCCTAGGAC GTTGCGCCAAG
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		GGTGGAAATC AAACGGGCGG CCGCAGAACA AAAACATCATC TCAGAAGAGG ATCTGAATTA A (SEQ ID NO:397)		GGACCAAGGT GGAAATCAAA CGG (SEQ ID NO:399)
DMS7325 (IFN α 2b- DOM7h- 11)	CDLPQTHSLGSRRT LMLLAQMRRISLFS CLKDRHDFGFPQE EFGNQFQKAETIPV LHEMIQQIFNLFST KDSSAAWDETLLD KFYTELYQQLNDL EACVIQGVGVETETP LMKEDSILAVRKY FQRITLYLKEKKYS PCAWEVVRAEIMR SFSLSSTNLQESLRS KETVAAPSDIQMT QSPSSLSASVGDRV TITCRASRPIGTTL WYQQKPGKAPKLL IWFGSRLQSGVPSR FSGSGSGTDFTLTIS SLQPEDFATYYCA QAGTHPTTFGQGT KVEIKR AAAEQKLISEEDL	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTTTC TTTGTTCTCTT GTCTAAAGGAC CGTCACGACTT CGGATTCCCTC AGGAAGAGTTT GGAAACCAATT CCAAAAAGCA GAAACTATTCC TGTCTTGCACG AAATGATCCAG CAAATATTCAA TTTGTTTTCTA CAAAGGACTC ATCAGCCGCTT GGGATGAAAC	CDLPQTHSLG SRRTLMLLA QMRRISLFSC LKDRHDFGFP QEEFGNQFQ KAETIPVLHE MIQQIFNLF TKDSSAAWD ETLLDKFYTE LYQQLNDLE ACVIQGVGV TETPLMKEDS ILAVRKYFQR ITLYLKEKKY SPCAWEVVR AEIMRSFSL TNLQESLSK ETVAAPSDIQ MTQSPSSLSA SVGDRVITC RASRPIGTTL SWYQQKPGK	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTTTC TTTGTTCTCTT GTCTAAAGGA CCGTCACGACT TCGGATTCCCT CAGGAAGAGT TTGGAAACCA ATTCCAAAAA GCAGAAACTA TTCCTGTCTTG CACGAAATGA TCCAGCAAATA TTCAATTTGTT TTCTACAAAGG ACTCATCAGCC GCTTGGGATGA

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	N* (SEQ ID NO:400)	TCTGTTAGATA AATTCTACACT GAACTATATCA ACAACTGAAC GATCTAGAGGC TTGCGTTATTC AGGGTGTAGG AGTTACTGAAA CTCCCCTAATG AAAGAAGATT CAATTCTAGCC GTTAGAAAATA CTTTCAGCGTA TCACATTGTAT TTAAAGGAAA AGAAATACTCC CCATGTGCATG GGAGGTGGTTA GAGCAGAAAT TATGAGGTCCT TCTCTCTTCT ACGAATTTGCA AGAATCTTTGA GATCTAAGGA AACCGTCGCTG CTCCATCTGAC ATCCAGATGAC CCAGTCTCCAT CCTCCCTGTCT GCATCTGTAGG	APKLLIWFGS RLQSGVPSRF SGSGSGTDFT LTISSLQPEDF ATYYCAQAG THPTTFGQGT KVEIKR (SEQ ID NO:402)	AACTCTGTTAG ATAAATTCTAC ACTGAACTATA TCAACAACCTGA ACGATCTAGA GGCTTGCGTTA TTCAGGGTGTA GGAGTTACTGA AACTCCCCTAA TGAAAGAAGA TTCAATTCTAG CCGTTAGAAA ATACTTTCAGC GTATCACATTG TATTTAAAGGA AAAGAAATAC TCCCCATGTGC ATGGGAGGTG GTTAGAGCAG AAATTATGAG GTCCTTCTCTC TTTCTACGAAT TTGCAAGAATC TTTGAGATCTA AGGAAACCGT CGCTGCTCCAT CTGACATCCAG ATGACCCAGTC TCCATCCTCCC TGTCTGCATCT
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	AGACCGTGTCA CCATCACTTGC CGGGCAAGTC GTCCGATTGGG ACGACGTTAAG TTGGTACCAGC AGAAACCAGG GAAAGCCCCTA AGCTCCTGATC TGGTTTGGTTC CCGGTTGCAAA GTGGGGTCCCA TCACGTTTCAG TGGCAGTGGAT CTGGGACAGAT TTCACCTCAC CATCAGCAGTC TGCAACCTGAA GATTTTGCTAC GTACTACTGTG CGCAGGCTGG GACGCATCCTA CGACGTTCGGC CAAGGGACCA AGGTGGAAAT CAAACGGGCG GCCGCAGAAC AAAACTCAT CTCAGAAGAG GATCTGAATT		GTAGGAGACC GTGTCACCATC ACTTGCCGGGC AAGTCGTCCGA TTGGGACGAC GTAAAGTTGGT ACCAGCAGAA ACCAGGGAAA GCCCCTAAGCT CCTGATCTGGT TTGGTTCCCGG TTGCAAAGTGG GGTCCCATCAC GTTTCAGTGGC AGTGGATCTGG GACAGATTTCA CTCTCACCATC AGCAGTCTGCA ACCTGAAGATT TTGCTACGTAC TACTGTGCGCA GGCTGGGACG CATCCTACGAC GTTCCGGCCAAG GGACCAAGGT GGAAATCAAA CGG (SEQ ID NO:403)
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		AA (SEQ ID NO:401)		
DMS7326 (IFN α 2b- DOM7h- 11-12)	CDLPQTHSLGSRRT LMLLAQMRRISLFS CLKDRHDFGFPQE EFGNQFQKAETIPV LHEMIQQIFNLFST KDSSAAWDETLLD KFYTELYQQNLNDL EACVIQGVGVETETP LMKEDSILAVRKY FQRITLYLKEKKYS PCAWEVVRAEIMR SFSLSSTNLQESLRS KETVAAPSDIQMT QSPSSLSASVGDRV TITCRASRPIGTML SWYQQKPGKAPKL LILFGSRLQSGVPS RFSGSGSGTDFTLT ISSLQPEDFATYYC AQAGTHPTTFGQG TKVEIKR AAAEQKLISEEDL N* (SEQ ID NO:404)	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTTTC TTTGTCTCTCTT GTCTAAAGGAC CGTCACGACTT CGGATTCCCTC AGGAAGAGTTT GGAAACCAATT CCAAAAAGCA GAAACTATTCC TGTCTTGCACG AAATGATCCAG CAAATATTCAA TTTGTTTTCTA CAAAGGACTC ATCAGCCGCTT GGGATGAAAC TCTGTAGATA AATTCTACACT GAACTATATCA ACAACTGAAC GATCTAGAGGC TTGCGTTATTC	CDLPQTHSLG SRRTLMLLA QMRRISLFSC LKDRHDFGFP QEEFGNQFQ KAETIPVLHE MIQQIFNLF TKDSSAAWD ETLLDKFYTE LYQQLNDLE ACVIQGVGV TETPLMKEDS ILAVRKYFQR ITLYLKEKKY SPCAWEVVR AEIMRSFSL TNLQESLSK ETVAAPSDIQ MTQSPSSLSA SVGDRVITC RASRPIGTML SWYQQKPGK APKLLILFGS RLQSGVPSRF SGSGSGTDFT LTISSLQPEDF ATYYCAQAG THPTTFGQGT	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA TTGATGTTATT AGCACAAATG CGTAGAATTTTC TTTGTCTCTCTT GTCTAAAGGA CCGTCACGACT TCGGATTCCCT CAGGAAGAGT TTGGAAACCA ATTCCAAAA GCAGAAACTA TTCCTGTCTTG CACGAAATGA TCCAGCAAATA TTCAATTTGTT TTCTACAAAGG ACTCATCAGCC GCTTGGGATGA AACTCTGTTAG ATAAATTCTAC ACTGAACTATA TCAACAACCTGA ACGATCTAGA GGCTTGCGTTA

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		AGGGTGTAGG AGTTACTGAAA CTCCCCTAATG AAAGAAGATT CAATTCTAGCC GTTAGAAAATA CTTTCAGCGTA TCACATTGTAT TTAAAGGAAA AGAAATACTCC CCATGTGCATG GGAGGTGGTTA GAGCAGAAAT TATGAGGTCCT TCTCTCTTCT ACGAATTTGCA AGAATCTTTGA GATCTAAGGA AACCGTCGCTG CTCCATCTGAC ATCCAGATGAC CCAGTCTCCAT CCTCCCTGTCT GCATCTGTAGG AGACCGTGTCA CCATCACTTGC CGGGCAAGTC GTCCGATTGGG ACGATGTTAAG TTGGTACCAGC	KVEIKR (SEQ ID NO:406)	TTCAGGGTGTA GGAGTTACTGA AACTCCCCTAA TGAAAGAAGA TTCAATTCTAG CCGTTAGAAA ATACTTTCAGC GTATCACATTG TATTTAAAGGA AAAGAAATAC TCCCCATGTGC ATGGGAGGTG GTTAGAGCAG AAATTATGAG GTCCTTCTCTC TTTCTACGAAT TTGCAAGAATC TTTGAGATCTA AGGAAACCGT CGCTGCTCCAT CTGACATCCAG ATGACCCAGTC TCCATCCTCCC TGTCTGCATCT GTAGGAGACC GTGTCACCATC ACTTGCCGGGC AAGTCGTCCGA TTGGGACGATG TTAAGTTGGTA
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		AGAAACCAGG GAAAGCCCCTA AGCTCCTGATC TTGTTTGGTTC CCGGTTGCAAA GTGGGGTCCCA TCACGTTTCAG TGGCAGTGGAT CTGGGACAGAT TTCACCTCTCAC CATCAGCAGTC TGCAACCTGAA GATTTTGCTAC GTACTACTGTG CGCAGGCTGG GACGCATCCTA CGACGTTCGGC CAAGGGACCA AGGTGGAAAT CAAACGGGCG GCCGCAGAAC AAAAACTCAT CTCAGAAGAG GATCTGAATT AA (SEQ ID NO:405		CCAGCAGAAA CCAGGGAAAG CCCCTAAGCTC CTGATCTTGTT TGGTTCCCGGT TGCAAAGTGG GGTCCCATCAC GTTTCAGTGGC AGTGGATCTGG GACAGATTTCA CTCTCACCATC AGCAGTCTGCA ACCTGAAGATT TTGCTACGTAC TACTGTGCGCA GGCTGGGACG CATCCTACGAC GTTCCGGCCAAG GGACCAAGGT GGAAATCAAA CGG (SEQ ID NO:407)
DMS7327 (IFN α 2b- DOM7h- 11-15)	CDLPQTHSLGSRRT LMLLAQMRRISLFS CLKDRHDFGFPQE EFGNQFQKAETIPV	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA	CDLPQTHSLG SRRTLMLLA QMRRISLFSC LKDRHDFGFP	TGCGACTTGCC ACAGACACAT AGTTTGGGATC AAGAAGAACA

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LHEMIQQIFNLFST	TTGATGTTATT	QEEFGNQFQ	TTGATGTTATT
KDSSAAWDETLLD	AGCACAAATG	KAETIPVLHE	AGCACAAATG
KFYTELYQQNLNDL	CGTAGAATTTTC	MIQQIFNLF	CGTAGAATTTTC
EACVIQGVGVETETP	TTTGTTCTCTT	TKDSSAAWD	TTTGTTCTCTT
LMKEDSILAVRKY	GTCTAAAGGAC	ETLLDKFYTE	GTCTAAAGGA
FQRITLYLKEKKYS	CGTCACGACTT	LYQQLNDLE	CCGTCACGACT
PCAWEVVRAEIMR	CGGATTCCCTC	ACVIQGVGV	TCGGATTCCCT
SFSLSTNLQESLRS	AGGAAGAGTTT	TETPLMKEDS	CAGGAAGAGT
KETVAAPSDIQMT	GGAAACCAATT	ILAVRKYFQR	TTGGAAACCA
QSPSSLSASVGDRV	CCAAAAAGCA	ITLYLKEKKY	ATTCCAAAAA
TITCRASRPIGTM	GAAACTATTCC	SPCAWEVVR	GCAGAAACTA
SWYQQKPGKAPKL	TGTCTTGCACG	AEIMRSFSL	TTCCTGTCTTG
LILAFSRLQSGVPS	AAATGATCCAG	TNLQESLSK	CACGAAATGA
RFSGSGSGTDFTLT	CAAATATTCAA	ETVAAPSDIQ	TCCAGCAAATA
ISSLQPEDFATYYC	TTTGTTTTCTA	MTQSPSSLSA	TTCAATTTGTT
AQAGTHPTTFGQG	CAAAGGACTC	SVGDRVITC	TTCTACAAAGG
TKVEIKR	ATCAGCCGCTT	RASRPIGTM	ACTCATCAGCC
AAAEQKLISEEDL	GGGATGAAAC	SWYQQKPGK	GCTTGGGATGA
N* (SEQ ID NO:408)	TCTGTAGATA	APKLLILAFS	AACTCTGTTAG
	AATTCTACACT	RLQSGVPSRF	ATAAATTCTAC
	GAACATATATCA	SGSGSGTDFT	ACTGAACATA
	ACAACATGAAC	LTISLQPEDF	TCAACAACATA
	GATCTAGAGGC	ATYYCAQAG	ACGATCTAGA
	TTGCGTTATTC	THPTTFGQGT	GGCTTGCGTTA
	AGGGTGTAGG	KVEIKR (SEQ	TTCAGGGTGTA
	AGTTACTGAAA	ID NO:410)	GGAGTTACTGA
	CTCCCCTAATG		AACTCCCCTAA
	AAAGAAGATT		TGAAAGAAGA
	CAATTCTAGCC		TTCAATTCTAG
	GTTAGAAAATA		CCGTTAGAAA

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	CTTTCAGCGTA TCACATTGTAT TTAAAGGAAA AGAAATACTCC CCATGTGCATG GGAGGTGGTTA GAGCAGAAAT TATGAGGTCCT TCTCTCTTCT ACGAATTTGCA AGAATCTTTGA GATCTAAGGA AACCGTCGCTG CTCCATCTGAC ATCCAGATGAC CCAGTCTCCAT CCTCCCTGTCT GCATCTGTAGG AGACCGTGTCA CCATCACTTGC CGGGCAAGTC GTCCGATTGGG ACGATGTTAAG TTGGTACCAGC AGAAACCAGG GAAAGCCCCTA AGCTCCTGATC CTTGCTTTTTC CCGTTTGCAAA GTGGGGTCCCA		ATACTTTCAGC GTATCACATTG TATTTAAAGGA AAAGAAATAC TCCCCATGTGC ATGGGAGGTG GTTAGAGCAG AAATTATGAG GTCCTTCTCTC TTTCTACGAAT TTGCAAGAATC TTTGAGATCTA AGGAAACCGT CGCTGCTCCAT CTGACATCCAG ATGACCCAGTC TCCATCCTCCC TGTCTGCATCT GTAGGAGACC GTGTCACCATC ACTTGCCGGGC AAGTCGTCCGA TTGGGACGATG TTAAGTTGGTA CCAGCAGAAA CCAGGGAAAG CCCCTAAGCTC CTGATCCTTGC TTTTTCCCGTT TGCAAAGTGG
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		TCACGTTTCAG TGGCAGTGGAT CTGGGACAGAT TTCACCTCTCAC CATCAGCAGTC TGCAACCTGAA GATTTTGCTAC GTACTACTGCG CGCAGGCTGG GACGCATCCTA CGACGTTTCGGC CAAGGGACCA AGGTGGAAAT CAAACGGG CG GCCGCAGAAC AAAACTCAT CTCAGAAGAG GATCTGAATT AA (SEQ ID NO:409)		GGTCCCATCAC GTTTCAGTGGC AGTGGATCTGG GACAGATTTCA CTCTCACCATC AGCAGTCTGCA ACCTGAAGATT TTGCTACGTAC TACTGCGCGCA GGCTGGGACG CATCCTACGAC GTTTCGGCCAAG GGACCAAGGT GGAAATCAAA CGG (SEQ ID NO:411)
--	--	--	--	--

The amino acid and nucleotide sequences highlighted in bold represents the cloning site and MYC tag. * represents the stop codon at the end of the gene.

5 Affinity Determination and Biophysical Characterisation:

To determine the binding affinity (K_D) of the AlbudAb-IFN α 2b fusion proteins to each serum albumin; purified fusion proteins were analysed by BIAcore over albumin (immobilised by primary-amine coupling onto CM5 chips; BIAcore) using fusion protein concentrations from 5000nM to 39nM (5000nM, 2500nM, 1250nM, 625nM,

10 312nM, 156nM, 78nM, 39nM) in HBS-EP BIAcore buffer.

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Table 12: Affinity to SA

AlbudAb	Fusion	Affinity to SA (nM)	Kd	Ka
		Rat		
DOM7h-14	IFN α 2b	350	4.500E-02	1.28E+05
DOM7h-14-10	IFN α 2b	16	4.970E-03	5.90E+05
DOM 7h-14-18	IFN α 2b	780	2.127E-01	5.80E+05
DOM 7h-14-19	IFN α 2b	1900	1.206E-01	7.96E+04
DOM 7h-11	IFN α 2b	6000	7.500E-01	nd
DOM 7h-11-12	IFN α 2b	1700	3.100E-01	1.30E+05
DOM 7h-11-15	IFN α 2b	200	1.660E-02	1.50E+05
		Cyno		
DOM 7h-14	IFN α 2b	60	1.32E-02	5.0E+05
DOM 7h-14-10	IFN α 2b	19	7.05E-03	4.50E+05
DOM 7h-14-18	IFN α 2b	no binding	no binding	no binding
DOM 7h-14-19	IFN α 2b	520	8.47E-02	2.73E+05
DOM 7h-11	IFN α 2b	3300	3.59E-01	1.20E+05
DOM 7h-11-12	IFN α 2b	630	3.45E-01	7.00E+05
DOM 7h-11-15	IFN α 2b	15	4.86E-03	3.60E+05
		Mouse		
DOM 7h-14	IFN α 2b	240	3.21E-02	1.50E+06
DOM 7h-14-10	IFN α 2b	60	3.45E-02	6.86E+05
DOM 7h-14-18	IFN α 2b	180	1.50E-01	9.84E+05

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DOM 7h-14-19	IFN α 2b	490	4.03E-02	1.19E+05
DOM 7h-11	IFN α 2b	6000	1.55E-01	nd
DOM 7h-11-12	IFN α 2b	150	9.49E-02	6.30E+05
DOM 7h-11-15	IFN α 2b	28	6.69E-03	2.80E+05
		Human		
DOM 7h-14	IFN α 2b	244	2.21E-02	9.89E+04
DOM 7h-14-10	IFN α 2b	32	6.58E-03	3.48E+05
DOM 7h-14-18	IFN α 2b	470	2.75E-01	6.15E+05
DOM 7h-14-19	IFN α 2b	350	4.19E-02	1.55E+05
DOM 7h-11	IFN α 2b	670	2.02E-01	7.00E+05
DOM 7h-11-12	IFN α 2b	500	1.66E-01	3.90E+05
DOM 7h-11-15	IFN α 2b	10	1.87E-03	3.50E+05

- When IFN α 2b is linked to the AlbudAb variants, in all cases the affinity of AlbudAb binding to serum albumin is reduced. DOM7h-14-10 and DOM7-11-15 retain improved
- 5 binding affinity to serum albumin across species compared to parent. DOM7h-11-12 also shows improved binding affinity to serum albumin across species compared to parent.

Table 13: Biophysical Characterisation

- 10 Biophysical Characterisation was carried out by SEC MALLS and DSC as described above for the single AlbudAbs.

AlbudAb	Fusion	DMS number	Biophysical parameters
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			SEC MALLS	DSC Tm(°C)
DOM 7h-14	IFN α 2b	DMS7321	M/D	58-65
DOM 7h-14-10	IFN α 2b	DMS7322	M/D	55-65
DOM 7h-14-18	IFN α 2b	DMS7323	M/D	55-65
DOM 7h-14-19	IFN α 2b	DMS7324	M/D	59-66
DOM 7h-11	IFN α 2b	DMS7325	M/D	65.8-66.2
DOM 7h-11-12	IFN α 2b	DMS7326	M/D	67-67.3
DOM 7h-11-15	IFN α 2b	DMS7327	M/D	56.3-66.2

M/D indicates a monomer/dimer equilibrium as detected by SEC MALLS

We observed expression for all clones in Tabale 13 in the range of 17.5 to 54 mg/L in
5 HEK293.

For IFN α 2b-DOM7h-14 and IFN α 2b-DOM7h-11 variants, favorable biophysical
parameters and expression levels were maintained during affinity maturation.

10

PK Determination for AlbudAb-IFN α 2bfusions

AlbudAbs IFN α 2b fusions DMS7321 (IFN α 2b-DOM7h-14) DMS7322 (IFN α 2b-
DOM7h-14-10) DMS7323 (IFN α 2b-DOM7h-14-18), DMS7324 (IFN α 2b-DOM7h-14-
15 19), DMS7325 (IFN α 2b-DOM7h-11), DMS7326 (IFN α 2b-DOM7h-11-12), DMS7327
(IFN α 2b-DOM7h-11-15) were expressed with the myc tag at 20-50mg quantities in
HEK293 cells and purified from culture supernatant using protein L affinity resin and
eluted with 100mM glycine pH2. The proteins were concentrated to greater than
1mg/ml, buffer exchanged into Dulbecco's PBS and endotoxin depleted using Q spin
20 columns (Vivascience).

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For Rat PK, IFN-AlbudAbs were dosed as single i.v injections at 2.0mg/kg using 3 rats per compound. Serum samples were taken at 0.16, 1, 4, 8, 24, 48, 72, 120, 168hrs.

Analysis of serum levels was by EASY ELISA according to manufacturers instructions

5 (GE Healthcare, catalogue number RPN5960).

For Mouse PK, DMS7322 (IFN2b-DOM7h-14-10) DMS7325 (IFN2b-DOM7h-11), DMS7326 (IFN2b-DOM7h-11-12), DMS7327 (IFN2b-DOM7h-11-15) all with myc tags were dosed as single i.v injections at 2.0mg/kg per dose group of 3 subjects and

10 serum samples taken at 10mins; 1h; 8h; 24h; 48h; 72h; 96h. Analysis of serum levels was by EASY ELISA according to manufacturers instructions (GE Healthcare, catalogue number RPN5960).

15

20 **Table 14:**

Species	AlbudAb	Fusion	Albumin K _D (nM)	PK parameters			
				AUC h x ug/ml	CL ml/h/kg	t _{1/2} h	V _z ml/kg
Rat	7h-14	IFN α 2b	350	832.1	2.4	27	94.5
	7h-14-10	IFN α 2b	16	1380.7	1.5	35.8	75.2
	7h-14-18	IFN α 2b	780	691.2	2.9	22.4	93.7
	7h-14-19	IFN α 2b	1900	969.4	2.2	25	78.7

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	7h-11	IFN α 2b	6000	327.9	6.5	11	101.9
	7h-11-12	IFN α 2b	1700	747.1	2.8	25.8	104.7
	7h-11-15	IFN α 2b	200	1118.7	1.8	39.5	103.6
mouse	7h-14	IFN α 2b	240	761.2	2.6	30.4	115.3
	7h-14-10	IFN α 2b	60	750.5	2.7	30.9	118.6
	7h-11	IFN α 2b	6000	493.9	4.0	8.8	51.2
	7h-11-12	IFN α 2b	150	439.6	4.5	21.5	140.9
	7h-11-15	IFN α 2b	28	971.8	2.1	33.6	99.6

Pharmacokinetic parameters derived from rat and mouse studies were fitted using a non-compartmental model. Key: AUC: Area under the curve from dosing time extrapolated to infinity; CL: clearance; t_{1/2}: is the time during which the blood concentration is halved; V_z: volume of distribution based on the terminal phase.

IFN α 2b –AlbudAbs were tested in rat and mouse. For all IFN α 2b -DOM7h-11 variant fusion proteins in both rat and mouse, t_{1/2} is improved compared to parent. The improvement in t_{1/2} correlates with the improved *in vitro* K_D to serum albumin. For IFN α 2b-DOM7h-14-10 variants, the improvement in *in vitro* K_D to serum albumin also correlated to an improvement in t_{1/2} in rat.

All IFN α 2b -AlbudAb fusion proteins exhibit a 5 to 10-fold decrease in the binding to RSA compared to the single AlbudAb. This effect is more pronounced (i.e. 10-fold) for the DOM7h-14 series than the DOM7h-11 series (only 5-fold decrease).

Example 8: Further AlbudAb fusions with proteins, peptides and NCEs.

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Various AlbudAbs fused to other chemical entities namely domain antibodies (dAbs), peptides and NCEs were tested. The results are shown in table 15.

Table 15:

Species	AlbudAb	Fusion	Albumin K _D (nM)	PK param- eters			
					AUC h x ug/ml	CL ml/h/kg	t1/2 h
Rat	DOM7h-14	Exendin-4	2400	18	57.1	11	901.9
	DOM7h-14-10	Exendin-4	19	43.6	23.1	22.1	740.3
	DOM7h-14-18	Exendin-4	16000	16.9	75.7	9.4	1002.5
	DOM7h-14-19	Exendin-4	17000	31.4	32.5	11.9	556.7
	DOM7h-11	Exendin-4	24000	6.1	168	7.1	1684.1
	DOM7h-11-12	Exendin-4	1400	24.2	59.9	13	1068.7
	DOM7h-11-15	Exendin-4	130	36.3	27.6	19.3	765.7
	DOM7h14-10	NCE-GGGGSC	62				
	DOM7h14-10	NCE-TVAAPSC	35				
Human	DOM7h-14	NCE	204				
mouse	DOM7h-11	DOM1m-		234	10.7	4.7	72.5

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		21-23					
	DOM7h- 11-12	DOM1m- 21-23		755	3.3	18	86.2
	DOM7h- 11-15	DOM1m- 21-23		1008	2.5	17.4	62.4

Key: DOM1m-21-23 is an anti-TNFR1 dAb, Exendin-4 is a peptide (a GLP-1 agonist) of 39 amino acids length. NCE, NCE-GGGGSC and NCE-TVAAPSC are described below.

5

Previously we have described the use of genetic fusions with an albumin-binding dAb (AlbudAb) to extend the PK half-life of anti-TNFR1 dAbs in vivo (see, eg, WO04003019, WO2006038027, WO2008149148). Reference is made to the protocols in these PCT applications. In the table above, DOM1m-21-23 is an anti-mouse TNFR1 dAb.

10

To produce genetic fusions of exendin-4 or with DOM7h-14 (or other AlbudAb) which binds serum albumin, the exendin-4-linker-AlbudAb sequence was cloned into the pTT-5 vector (obtainable from CNRC, Canada). In each case the exendin-4 was at the 5' end of the construct and the dAb at the 3' end. The linker was a (G₄S)₃ linker. Endotoxin-free DNA was prepared in E.coli using alkaline lysis (using the endotoxin-free plasmid Giga kit, obtainable from Qiagen CA) and used to transfect HEK293E cells (obtainable from CNRC, Canada). Transfection was into 250ml/flask of HEK293E cells at 1.75x10⁶ cells/ml using 333ul of 293fectin* (Invotrogen) and 250ug of DNA per flask and expression was at 30°C for 5 days. The supernatant was harvested by centrifugation and purification was by affinity purification on protein L. Protein was batch bound to the resin, packed on a column and washed with 10 column volumes of PBS. Protein was eluted with 50ml of 0.1M glycine pH2 and neutralised with Tris pH8.. Protein of the expected size was identified on an SDS-PAGE gel.

25

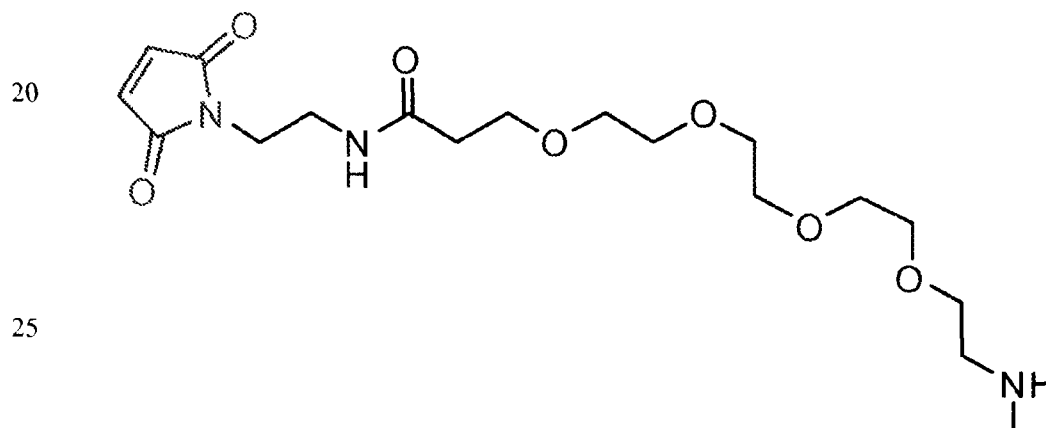
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NCE Albudab fusions:

A new chemical entity (NCE) AlbudAb fusion was tested. The NCE, a small molecule ADAMTS-4 inhibitor was synthesised with a PEG linker (PEG 4 linker (ic 4 PEG molecules before the maleimide) and a maleimide group for conjugation to the AlbudAb. Conjugation of the NCE to the AlbudAb is via an engineered cystine residue at amino acid position R108C, or following a 5 amino acid (GGGGSC) or 6 amino acid (TVAAPSC) spacer engineered at the end of the AlbudAb. Briefly, the AlbudAb was reduced with TCEP (Pierce, Catalogue Number 77720), desalted using a PD10 column (GE healthcare) into 25mM Bis-Tris, 5mM EDTA, 10% (v/v) glycerol pH6.5. A 5 fold molar excess of maleimide activated NCE was added in DMSO not to exceed 10% (V/V) final concentration. The reaction was incubated over night at room temperature and dialysed extensively into 20mM Tris pH7.4

15

PEG linker:



Sequences:

30 DOM7h-14-10 R108C:

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DIQMTQSPSSLSASVGDRVITTCRASQWIGSQLSWYQQKPGKAPKLLIMWRSSL
 QSGVPSRFSGSGSGTDFLTISLQPEDFATYYCAQGLRHPKTFGQGTKVEIKC
 (SEQ ID NO:412)

5 Nucleotide:

GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACC
 GTGTCACCATCACTTGCCGGGCAAGTCAGTGGATTGGGTCTCAGTTATCTTG
 GTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCATGTGGCGTTC
 CTCGTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAGTGGATCTGGGAC
 10 AGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCTACGTAC
 TACTGTGCTCAGGGTTTGAGGCATCCTAAGACGTTTCGGCCAAGGGACCAAG
 GTGGAAATCAAATGC (SEQ ID NO:413)

See table 5 for the sequences of DOM7h-14-10/TVAAPSC and DOM7h-14-
 15 10/GGGGSC (ie, DOM7h-14-10/G4SC).

NCE-AlbudAbs DOM7h-14-10 GGGGSC and DOM7h14-10 TVAAPSC, exhibit a 5 to
 10 fold decrease in *in vitro* affinity (K_D) to RSA as determined by BIAcore when fused
 to the chemical entity. PK data are not available for these molecules yet.

20

dAb-Albudab fusion: the 2 DOM7h-11 AlbudAbs with the highest affinity to RSA
 experience a 2-fold decrease in affinity to RSA as on BIAcore when fused to a
 therapeutic domain antibody (DOM1m-21-23) compared to the unfused AlbudAb. The
 DOM7h-11 clone shows a micromolar K_D when fused (2.8uM) as well as when unfused
 25 (~5uM).

Exendin 4-AlbudAb fusion: the effect of fusing the AlbudAbs to a peptide on the
 binding ability to RSA is about 10-fold, apart from DOM7h-14-10, which only shows a
 4-fold decrease in binding. The effect, however, is more pronounced for the DOM7h-14
 30 series (except DOM7h-14-10) than it appears to be for the DOM7h-11 series.

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For all the above data, the T1/2 of the fusion increased with improved affinity to the species' SA.

- 5 We generally classify Albudab-therapeutics as being therapeutically amenable (for treatment and/or prophylaxis of diseases, conditions or indications) when the AlbudAb-drug fusions show an affinity range (K_D) of from 0.1 nM to 10 mM for serum albumin binding.
- 10 We define the therapeutic ranges of AlbudAbs and AlbudAb fusions (Protein-AlbudAbs for example IFNa2b-DOM7h-14-10; Peptide-AlbudAbs for example Exendin-4-DOM7h-14-10; dAb-AlbudAbs for example DOM1m21-23-DOM7h11-15; NCE-AlbudAb for example ADAMTS-4-DOM7h-14-10) as follows: Affinity (K_D) ranges that are useful for therapy of chronic or acute conditions, diseases or indications are
- 15 shown. Also shown are affinity ranges marked as "intermediate". AlbudAbs and fusions in this range have utility for chronic or acute diseases, conditions or indications. In this way, the affinity of the AlbudAb or fusion for serum albumin can be tailored or chosen according to the disease, condition or indication to be addressed. As described above, the invention provides AlbudAbs with affinities that allow for each AlbudAb to
- 20 be categorised as "high affinity", "medium affinity" or "low affinity", thus enabling the skilled person to select the appropriate AlbudAb of the invention according to the therapy at hand. See Figure 2.

25

Example 9: DOM7h-11-15^{S12P} Sequences

Amino Acid Sequence of DOM7h-11-15^{S12P}

30

DIQMTQSPSSLPASVGDRVTITCRASRPIGTMLSWYQQKPGKAPKLLILAFSRLQ
SGVPSRFGSGSGTDFTLTISSLQPEDFATYYCAQAGTHPTTFGQGTKVEIKR
(SEQ ID NO: 414)

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An aspect of the invention provides a nucleic acid comprising the nucleotide sequence of DOM7h-11-15^{S12P} or a nucleotide sequence that is at least 80% identical to said

- 5 selected sequence. DOM7h-11-15^{S12P} was produced using the following nucleic acid sequence (the underlined C denotes the change (versus the nucleic acid encoding DOM7h-11-15) leading to a proline at position 12):-

10 GACATCCAGATGACCCAGTCTCCATCCTCCCTGCCTGCATCTGTAGGAGACC
 GTGTCACCATCACTTGCCGGGCAAGTCGTCCGATTGGGACGATGTTAAGTTG
 GTACCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCCTTGCTTTTCC
 CGTTTGCAAAGTGGGGTCCCATCACGTTTCAGTGGCAGTGGATCTGGGACA
 GATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCTACGTACT
 15 ACTGCGCGCAGGCTGGGACGCATCCTACGACGTTTCGGCCAAGGGACCAAGG
 TGGAAATCAAACGG (SEQ ID NO: 415)

DOM7h-11-15^{S12P} was constructed by using DOM7h-11-15 as a template in a PCR where a primer was used to introduce the S12P mutation. The primer sequence is:-

20 GCAACAGCGTCGACGGACATCCAGATGACCCAGTCTCCATCCTCCCTGCCTG
 CATCTGTAGG (SEQ ID NO: 416).

- An alternative aspect of the invention provides a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 415 or a nucleotide sequence that is at least 80% identical to
- 25 said selected sequence. In one embodiment, DOM7h-11-15^{S12P} is encoded by, and expressed from, a vector that contains a linker region and a C-terminal sequence encoding a protein or peptide drug or a single variable domain or other antibody fragment to make the in-line protein fusion product. The linker, in one embodiment, comprises the amino acid sequence TVA, eg, TVAAPS. Other aspects of the invention
- 30 are a vector comprising the nucleic acid; and an isolated host cell comprising the vector. The invention also provides a method of treating or preventing a disease or disorder in a patient, comprising administering at least one dose of DOM7h-11-15^{S12P} to said patient.

What is claimed is:

1. An anti-serum albumin immunoglobulin single variable domain comprising the amino acid sequence of SEQ ID NO: 412 or having up to 3 amino acid changes compared to SEQ ID NO:412, wherein CDR1 of the single variable domain is identical to SEQ ID NO:359, CDR2 of the single variable domain is identical to SEQ ID NO:360 and CDR3 of the single variable domain is identical to SEQ ID NO:361,excluding SEQ ID NO: 1.
2. An anti-serum albumin immunoglobulin single variable domain comprising the amino acid sequence of SEQ ID NO: 412.
3. The anti-serum albumin immunoglobulin single variable domain of claim 1 or 2, comprising a binding site that specifically binds human serum albumin with a dissociation constant (KD) of from about 0.1 to about 10000 nM, as determined by surface plasmon resonance.
4. The anti-serum albumin immunoglobulin single variable domain of claim 3, wherein KD is from about 1 to about 6000 nM.
5. The anti-serum albumin immunoglobulin single variable domain of any one of claims 1 to 4, comprising a binding site that specifically binds human serum albumin with an off-rate constant (K_d) of from about 1.5×10^{-4} to about 0.1 sec^{-1} , as determined by surface plasmon resonance.
6. The anti-serum albumin immunoglobulin single variable domain of claim 5, wherein K_d is from about 3×10^{-4} to about 0.1 sec^{-1} .
7. The anti-serum albumin immunoglobulin single variable domain of any one of claims 1 to 6, comprising a binding site that specifically binds human serum albumin with an on-rate constant (K_a) of from about 2×10^6 to about $1 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$, as determined by surface plasmon resonance.
8. The anti-serum albumin immunoglobulin single variable domain of claim 7, wherein K_a is from about 1×10^6 to about $2 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$.

9. The anti-serum albumin immunoglobulin single variable domain of claim 1 or 2, comprising a binding site that specifically binds *Cynomolgus* monkey serum albumin with a dissociation constant (KD) of from about 0.1 to about 10000 nM, as determined by surface plasmon resonance.
10. The anti-serum albumin immunoglobulin single variable domain of claim 9, wherein KD is about 1 to about 6000 nM.
11. The anti-serum albumin immunoglobulin single variable domain of claim 1, 2, 9 or 10, comprising a binding site that specifically binds *Cynomolgus* monkey serum albumin with an off-rate constant (K_d) of from about 1.5×10^{-4} to about 0.1 sec^{-1} , as determined by surface plasmon resonance.
12. The anti-serum albumin immunoglobulin single variable domain of claim 11, wherein K_d is about 3×10^{-4} to about 0.1 sec^{-1} .
13. The anti-serum albumin immunoglobulin single variable domain of any one of claims 1, 2, 9, 10, 11 and 12, comprising a binding site that specifically binds *Cynomolgus* monkey serum albumin with an on-rate constant (K_a) of from about 2×10^6 to about $1 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$, as determined by surface plasmon resonance.
14. The anti-serum albumin immunoglobulin single variable domain of claim 1 or 2, comprising a binding site that specifically binds human serum albumin and *Cynomolgus* monkey serum albumin, each with a dissociation constant (KD) of from about 0.1 to about 10000 nM, as determined by surface plasmon resonance.
15. The anti-serum albumin immunoglobulin single variable domain of claim 14, wherein KD is about 1 to about 6000 nM.
16. The anti-serum albumin immunoglobulin single variable domain of claim 14 or 15, comprising a binding site that specifically binds human serum albumin and *Cynomolgus* monkey serum albumin, each with an off-rate constant (K_d) of from about 1.5×10^{-4} to about 0.1 sec^{-1} , as determined by surface plasmon resonance.

17. The anti-serum albumin immunoglobulin single variable domain of claim 16, wherein K_d is about 3×10^{-4} to about 0.1 sec^{-1} .
18. The anti-serum albumin immunoglobulin single variable domain of any one of claims 14 to 17, comprising a binding site that specifically binds human serum albumin and *Cynomolgus* monkey serum albumin, each with an on-rate constant (K_a) of from about 2×10^6 to about $1 \times 10^4 \text{ M}^{-1}\text{sec}^{-1}$, as determined by surface plasmon resonance.
19. An anti-serum albumin immunoglobulin single variable domain of any one of claims 1 to 18, wherein the variable domain is conjugated to a drug.
20. A fusion protein comprising a polypeptide or peptide drug fused to an immunoglobulin single variable domain according to any one of claims 1 to 18.
21. A composition comprising an immunoglobulin single variable domain of any one of claims 1 to 19, or a fusion protein of claim 20 and a pharmaceutically acceptable diluent, carrier, excipient or vehicle.
22. A nucleic acid comprising a nucleotide sequence encoding an immunoglobulin single variable domain according to any one of claims 1 to 18 or a fusion protein of claim 20.
23. A nucleic acid comprising the nucleotide sequence of SEQ ID NO:413.
24. A vector comprising the nucleic acid of claim 22 or 23.
25. An isolated host cell comprising the vector of claim 24.

[illegible]

[illegible]

human	kinetics based on DOM7h-14 and DOM7h-11 lineage (ranges supported by data)		
	overall range		
	KD: 1 to 10000		
	Kd: 1.5e-4 to 0.1 ; Ka: 2e6 to 1e4		
therapeutic ranges	chronic	intermediate	acute
	high affinity	medium affinity	low affinity
	KD: 0.1-400	KD: 400-2000	KD: 2000-10000
	Kd: 1.5e-4 to 8e-3 ; Ka: 1e6 to 5e4	Kd: 8e-3 to 0.08 ; Ka: 2e4 to 5e4	Kd: 0.08 to 0.1 ; Ka: 5e4 to 1e4
optional ranges	KD: 1-200	KD: 400-1500	KD: 2000-6000
	Kd: 3e-4 to 2e-3 ; Ka: 1e6 to 5e4	Kd: 8e-3 to 0.08 ; Ka: 2e4 to 6e4	Kd: 0.08 to 0.1 ; Ka: 5e4 to 2e4
Examples	DOM7h-11-15, DOM7h-14, DOM7h-14-10, DOM7h-14-18, DOM7h-14-19, DOM7h-11-18, DOM7h-11-19, DMS7321, DMS7322, DMS7324, DMS7327	DMS7325, DMS7326, DMS7323	DOM7h-11

Figure 2A

Cyno			
	overall range		
	KD: 1 to 10000		
	KD: 1.5e-4 to 0.1 ; Ka: 2e6 to 1e4		
therapeutic ranges	chronic	intermediate	acute
	high affinity	medium affinity	low affinity
	KD: 0.1-400	KD: 400-2000	KD: 2000-10000
	Kd: 1.5e-4 to 8e-3 ; Ka: 2e6 to 2e4	Kd: 8e-3 to 0.08 ; Ka: 2e4 to 5e4	Kd: 0.08 to 0.1 ; Ka: 5e4 to 1e4
optional ranges	KD: 1-200	KD: 400-1500	KD: 2000-6000
	Kd: 3e-4 to 2e-3; Ka: 1e6 to 1e4	Kd: 2e-3 to 0.05; Ka: 2e4 to 1e4	Kd: 0.08 to 0.1 ; Ka: 5e4 to 2e4
Examples	DMS7327; DOM7h-11-15; DOM7h-14; DOM7h-14-10; DOM7h-14-18; DOM7h-14-19, DOM7h-14-28, DOM7h-14-36 DMS7321; DMS7322	DOM7h-11; DMS7326; DMS7324;	DOM7h11-12, DOM7h-11-18 DMS7325

Figure 2B

Rat			
	overall range		
	KD: 1 to 10000		
	KD: 2e-3 to 0.15 ; Ka: 2e6 to 1e4		
therapeutic ranges	chronic	intermediate	acute
	high affinity KD: 1-300	medium affinity KD: 300-2000	low affinity KD: 2000-10000
	Kd: 2e-3 to 5e-2 ; Ka: 2e6 to 2e5	Kd: 5e-2 to 0.09 ; Ka: 2e5 to 4.5e4	Kd: 0.09 to 0.15 ; Ka: 4.5e4 to 1.5e4
optional ranges	KD: 20-200	KD: 400-1800	KD: 2000-6000
	Kd: 9e-3 to 2e-2 ; Ka: 1e6 to 1e5	Kd: 4e-2 to 0.09; Ka: 1e5 to 5e4	Kd: 0.1 to 0.14 ; Ka: 5e4 to 3e4
Examples	DOM7h-11-15; DOM7h-11-12; DOM7h-11-18, DOM7h-11-19, DOM7h-14-28, DOM7h-14-36, DOM7h-14 DMS7327; DMS7322	DOM7h-14-18; DOM7h-14-19; DMS7321; DMS7323, DMS7324, DMS7326,,	DMS7325; DOM7h-11;

Figure 2C

[illegible]