

sample preparation (which can include, for example, polypeptide denaturation, reduction, alkylation, and digestion); (2) separating the digested polypeptides by LC and detecting them by MS; and (3) analysis of the data for targeted CQAs and detection of new signal (*i.e.*, peaks) when compared to a reference standard.

[0005] CQAs are chemical, physical, or biological properties that are present within a specific value or range values. For example, for large polypeptide therapeutic molecules, physical attributes and modifications of amino acids (the building blocks of polypeptides) are important CQAs that are monitored during and after manufacturing, as well as during drug development. Unlike conventional analytical assays that track changes in peak size and peak shape of whole or partial polypeptides, MAM detects specific CQAs at the amino acid level.

[0006] Analysis of the glycan profile of a polypeptide therapeutic is often a CQA.*e.g.* This is especially true in the case of biosimilar products, where the glycosylation profile of the biosimilar product must be comparable to that of the innovator product. Known processes for performing glycan assays require a sample of a product to be manually collected, delivered to a testing laboratory, and manually concentrated, purified,*e.g.* and prepared for analysis. The typical turnaround time for these known, manually operated, processes is about five days. This passage of time drives costs and delays in the development of drugs (innovator and biosimilar) and eventual drug release. For example, delays of five days accumulate during drug development, for example, when optimizing culture conditions for optimal glycosylation, impeding delivery of important and new polypeptide pharmaceuticals to patients. Furthermore, such delays result in profiles determined after manufacturing, resulting in re-manufacturing products that do not meet specifications as opposed to adjusting manufacturing parameters in real time. Thus, there is a need for efficient and faster methods to facilitate glycan analysis, including sample preparation for such analyses.

SUMMARY

[0007] One example of the present disclosure provides a method for preparing a sample in real-time for glycan analysis. The method includes the steps of: (a) moving a sample

comprising polypeptides to a polypeptide-binding column via a holding coil; (b) binding polypeptides in the sample to the polypeptide-binding column; (c) moving glycanases to the polypeptide-binding column via the holding coil to release glycans from the bound polypeptides; (d) moving a carrier solution to the polypeptide-binding column, via the holding coil, and through the polypeptide-binding column, thereby moving the released glycans out of the first polypeptide column; (e) mixing the released glycans with a glycan-labeling reagent downstream of the polypeptide-binding column; (f) moving the mixture of the released glycans and the glycan-labeling reagent to a reaction coil arranged downstream of the polypeptide-binding column; (g) incubating the mixture of the released glycans and the glycan-labeling reagent in the reaction coil, thereby labeling the glycans; (h) moving the mixture to a cooling coil arranged downstream of the reaction coil; (i) reducing a temperature of the mixture via the cooling coil; (j) moving the cooled mixture to a glycan-binding column arranged downstream of the cooling coil; (k) binding the labeled glycans to the glycan-binding column; and (l) moving an elution buffer to the glycan-binding column and through the glycan-binding column to elute the labeled glycans bound to the glycan-binding column.

[0007a] In one aspect, the present disclosure refers to a method for preparing a sample in real-time for glycan analysis, the method comprising the steps of: (a) moving a sample comprising polypeptides to a polypeptide-binding column (112) via a holding coil (108); (b) binding polypeptides in the sample to the polypeptide-binding column; (c) moving glycanases to the polypeptide-binding column via the holding coil to release glycans from the bound polypeptides; (d) moving a carrier solution to the polypeptide-binding column, via the holding coil, and through the polypeptide-binding column, thereby moving the released glycans out of the polypeptide-binding column; (e) mixing the released glycans with a glycan-labeling reagent downstream of the polypeptide-binding column; (f) moving the mixture of the released glycans and the glycan-labeling reagent to a reaction coil (120) arranged downstream of the polypeptide-binding column; (g) incubating the mixture of the released glycans and the glycan-labeling reagent in the reaction coil, thereby labeling the glycans; (h) moving the mixture to a cooling coil (152) arranged downstream of the reaction coil; (i) reducing a temperature of the mixture via the cooling coil; (j) moving the cooled mixture to a glycan-binding column (124) arranged downstream of the cooling coil; (k) binding the labeled glycans to the glycan-binding column; and (l) moving an elution buffer to the glycan-binding column and through the glycan-binding column to elute the labeled glycans bound to the glycan-binding column; wherein one or more of (a), (c), (d), (e), (f), (h), (j), and (l) are performed automatically.

[0008] In another aspect, the present disclosure refers to a method for preparing a sample in real-time for glycan analysis in a closed system including a multi-port valve (104), a holding coil (108) upstream of the multi-port valve, a polypeptide-binding column fluidly coupled to and downstream of a first port of the multi-port valve, a reaction coil arranged downstream of the polypeptide-binding column (112), a cooling coil (152) arranged downstream of the reaction coil (120), and a glycan-binding column (124) arranged downstream of the cooling coil and fluidly coupled to and downstream of a second port of the multi-port valve, the method comprising: (a) moving, via a controller (132) communicatively coupled to the closed system, a sample comprising polypeptides from a vessel containing the polypeptides to the holding coil; (b) positioning, via the controller, the multi-port valve in a first position in which the holding coil is fluidly coupled to the polypeptide-binding column via the first port of the multi-port valve, such that the sample flows to the polypeptide-binding column, whereby substantially all of the polypeptides in the sample bind to the first polypeptide column; (c) when the multi-port valve is in the first position, moving, via the

controller, glycanases to the polypeptide-binding column via the holding coil to release glycans from the bound polypeptides, and then moving, via the controller, a carrier solution to the polypeptide-binding column, via the holding coil, and through the polypeptide-binding column, thereby moving the released glycans out of the polypeptide-binding column; (d) moving, via the controller, the released glycans toward the reaction coil; (e) moving, via the controller, a glycan labeling reagent toward the released glycans prior to reaching the reaction coil, such that the glycan labeling reagent mixes with the released glycans and the enzymes; (f) moving, via the controller, the mixture to the reaction coil, whereby the glycans in the mixture are labeled; (g) moving, via the controller, the mixture to a cooling coil arranged downstream of the reaction coil, thereby reducing a temperature of the mixture; (h) moving, via the controller, the cooled mixture to a glycan column arranged downstream of the cooling coil, whereby substantially all of the labeled glycans bind to the glycan-binding column; (i) positioning, via the controller, the multi-port valve in a second position in which the glycan-binding column is fluidly coupled to a source of elution buffer solution via the second port of the multi-port valve; (j) when the multi-port valve is in the second position, moving, via the controller, the elution buffer from the elution buffer source to the glycan-binding column, and through the glycan-binding column, thereby eluting glycans bound to the glycan-binding column; and (k) moving, via the controller, the eluted glycans to a glycan analysis device.

[0008a] In yet another aspect the present disclosure provides a closed system for preparing a sample in real-time for glycan analysis, the closed system comprising: a vessel (136) adapted to contain polypeptides; a holding coil (108) fluidly coupled to the bioreactor and arranged to receive a sample of the polypeptides from the bioreactor; a multi-port valve (104) fluidly coupled to and located downstream of the holding coil; a polypeptide-binding column (112) fluidly coupled to the multi-port valve and arranged to receive the sample from the holding coil via a first port of the multi-port valve; a glucanase source fluidly coupled to the multi-port valve and arranged to supply glucanases to the polypeptide-binding column, such that the glucanases are infused with the polypeptides bound to the polypeptide-binding column; a carrier solution source fluidly coupled to the multi-port valve and arranged to supply a carrier solution to the polypeptide-binding column, wherein the carrier solution is adapted to release and carry the glycans from the polypeptide-binding column; a first pump (140) arranged downstream of the polypeptide-binding column to direct a glycan labeling reagent toward the released glycans carried from the polypeptide-binding column, such that the glycan labeling reagent mixes with the glycans; a reaction coil (120) arranged downstream of the polypeptide-binding column and the first pump, the reaction coil adapted to receive the mixture comprising the glycan labeling reagent and the released glycans and to permit labeling of the released glycans; a cooling coil (152) arranged downstream of the reaction coil and adapted to receive the mixture from the reaction coil, the cooling coil configured to reduce a temperature of the mixture; a glycan-binding column (124) fluidly coupled to the cooling coil and to the multi-port valve via a second port of the multi-port valve, the glycan-binding column configured to bind substantially all of the labeled glycans, the glycan-binding column adapted to receive an elution buffer solution via the second port of the multi-port valve, wherein the elution buffer solution elutes bound labeled glycans and carries the eluted labeled glycans to a glycan analysis device downstream of the glycan-binding column.

[0009] In another aspect the present disclosure provides a closed system for preparing a sample in real-time for glycan analysis, the closed system comprising: a multi-port valve (104), a holding coil (108) upstream of the multi-port valve, a polypeptide-binding column (112) fluidly coupled to and downstream of a first

port of the multi-port valve, a reaction coil (120) arranged downstream of the polypeptide-binding column, a cooling coil (152) arranged downstream of the reaction coil, a glycan-binding column (124) fluidly coupled to and downstream of the cooling coil, the glycan-binding column fluidly coupled to the multi-port valve via a second port of the multi-port valve, and a controller (132) communicatively coupled to the multi-port valve and comprising a memory, a processor, and logic stored on the memory and executable by the processor to: (a) move a sample of a product containing polypeptides to the holding coil; (b) position the multi-port valve in a first position in

CLAIMS

1. A method for preparing a sample in real-time for glycan analysis, the method comprising the steps of:
 - (a) moving a sample comprising polypeptides to a polypeptide-binding column (112) via a holding coil (108);
 - (b) binding polypeptides in the sample to the polypeptide-binding column;
 - (c) moving glycanases to the polypeptide-binding column via the holding coil to release glycans from the bound polypeptides;
 - (d) moving a carrier solution to the polypeptide-binding column, via the holding coil, and through the polypeptide-binding column, thereby moving the released glycans out of the polypeptide-binding column;
 - (e) mixing the released glycans with a glycan-labeling reagent downstream of the polypeptide-binding column;
 - (f) moving the mixture of the released glycans and the glycan-labeling reagent to a reaction coil (120) arranged downstream of the polypeptide-binding column;
 - (g) incubating the mixture of the released glycans and the glycan-labeling reagent in the reaction coil, thereby labeling the glycans;
 - (h) moving the mixture to a cooling coil (152) arranged downstream of the reaction coil;
 - (i) reducing a temperature of the mixture via the cooling coil;
 - (j) moving the cooled mixture to a glycan-binding column (124) arranged downstream of the cooling coil;
 - (k) binding the labeled glycans to the glycan-binding column; and
 - (l) moving an elution buffer to the glycan-binding column and through the glycan-binding column to elute the labeled glycans bound to the glycan-binding column;
- wherein one or more of (a), (c), (d), (e), (f), (h), (j), and (l) are performed automatically.

2. The method of claim 1, wherein (a) through (l) are performed in a closed system.
3. The method of claim 1 or 2, wherein:
the method further comprises, after (e) and before (f), moving the mixture to a vacuum apparatus (150) arranged downstream of the cooling coil and upstream of the glycan-binding column, and, using the vacuum apparatus, substantially removing gas bubbles from the mixture of the released glycans and the glycan-labeling reagent; and/or
the method further comprises, after (l), moving the eluted glycans through a mixing chamber (157) arranged downstream of the glycan-binding column, and adjusting an elution buffer component of the labeled glycans to match a starting chromatographic mobile phase condition; and/or
- (a) comprises moving the sample from a vessel (136) containing the sample to the polypeptide-binding column; and/or
(g) comprises fluorescently labeling the glycans with the glycan-labeling reagent; and/or
(g) comprises applying heat to the mixture in the reaction coil; and/or
- the method further comprises (m) moving the eluted glycans from the glycan-binding column to a glycan analysis device.
4. The method of claim 3, wherein the vessel comprises a bioreactor.
5. The method of claim 3 or 4, wherein the method further comprises (n) separating and quantitating the glycans using the glycan analysis device.
6. The method of any one of the preceding claims, further comprising, moving a valve (198) fluidly coupled to and located downstream of the polypeptide-

binding column to a first position in which the valve directs a remainder of the sample that flows through the polypeptide-binding column to a waste chamber.

7. The method of claim 6, further comprising, prior to (e), moving the valve to a second position in which the first valve directs the released glycans from and out of the polypeptide-binding column toward the glycan-labeling reagent.

8. A method for preparing a sample in real-time for glycan analysis in a closed system comprising a multi-port valve (104), a holding coil (108) upstream of the multi-port valve, a polypeptide-binding column (112) fluidly coupled to and downstream of a first port of the multi-port valve, a reaction coil (120) arranged downstream of the polypeptide-binding column, a cooling coil (152) arranged downstream of the reaction coil, and a glycan-binding column (124) arranged downstream of the cooling coil and fluidly coupled to and downstream of a second port of the multi-port valve, the method comprising:

(a) moving, via a controller (132) communicatively coupled to the closed system, a sample comprising polypeptides from a vessel containing the polypeptides to the holding coil;

(b) positioning, via the controller, the multi-port valve in a first position in which the holding coil is fluidly coupled to the polypeptide-binding column via the first port of the multi-port valve, such that the sample flows to the polypeptide-binding column, whereby substantially all of the polypeptides in the sample bind to the first polypeptide column;

(c) when the multi-port valve is in the first position, moving, via the controller, glycanases to the polypeptide-binding column via the holding coil to release glycans from the bound polypeptides, and then moving, via the controller, a carrier solution to the polypeptide-binding column, via the holding coil, and through the polypeptide-binding column, thereby moving the released glycans out of the polypeptide-binding column;

(d) moving, via the controller, the released glycans toward the reaction coil;

(e) moving, via the controller, a glycan labeling reagent toward the released glycans prior to reaching the reaction coil, such that the glycan labeling reagent mixes with the released glycans and the enzymes;

(f) moving, via the controller, the mixture to the reaction coil, whereby the glycans in the mixture are labeled;

(g) moving, via the controller, the mixture to a cooling coil arranged downstream of the reaction coil, thereby reducing a temperature of the mixture;

(h) moving, via the controller, the cooled mixture to a glycan column arranged downstream of the cooling coil, whereby substantially all of the labeled glycans bind to the glycan-binding column;

(i) positioning, via the controller, the multi-port valve in a second position in which the glycan-binding column is fluidly coupled to a source of elution buffer solution via the second port of the multi-port valve;

(j) when the multi-port valve is in the second position, moving, via the controller, the elution buffer from the elution buffer source to the glycan-binding column, and through the glycan-binding column, thereby eluting glycans bound to the glycan-binding column; and

(k) moving, via the controller, the eluted glycans to a glycan analysis device.

9. The method of claim 8, wherein:

the method further comprises, after (e) and before (f), moving, via the controller, the mixture to a vacuum apparatus (150) arranged downstream of the polypeptide-binding column and upstream of the reaction coil, thereby substantially removing gas bubbles from the mixture; and/or

the method further comprises, after (j) and before (k), moving, via the controller, the eluted glycans through a mixing chamber (157) arranged downstream of the glycan-binding column and upstream of the glycan analysis device; and/or

the method further comprises controlling, via the processor, the polypeptide-binding column to maintain the polypeptide-binding column at a temperature of approximately 38 degrees Celsius; and/or

the method further comprises controlling, via the processor, the reaction coil to maintain the reaction coil at a temperature of approximately 80 degrees Celsius; and/or

(f) comprises moving, via the controller, the mixture to the reaction coil, whereby the glycans in the mixture are fluorescently labeled.

10. A closed system for preparing a sample in real-time for glycan analysis, the closed system comprising:

a vessel (136) adapted to contain polypeptides;

a holding coil (108) fluidly coupled to the bioreactor and arranged to receive a sample of the polypeptides from the bioreactor;

a multi-port valve (104) fluidly coupled to and located downstream of the holding coil;

a polypeptide-binding column (112) fluidly coupled to the multi-port valve and arranged to receive the sample from the holding coil via a first port of the multi-port valve;

a glucanase source fluidly coupled to the multi-port valve and arranged to supply glucanases to the polypeptide-binding column, such that the glucanases are infused with the polypeptides bound to the polypeptide-binding column;

a carrier solution source fluidly coupled to the multi-port valve and arranged to supply a carrier solution to the polypeptide-binding column, wherein the carrier solution is adapted to release and carry the glycans from the polypeptide-binding column;

a first pump (140) arranged downstream of the polypeptide-binding column to direct a glycan labeling reagent toward the released glycans carried from the polypeptide-binding column, such that the glycan labeling reagent mixes with the glycans;

a reaction coil (120) arranged downstream of the polypeptide-binding column and the first pump, the reaction coil adapted to receive the mixture comprising the glycan labeling reagent and the released glycans and to permit labeling of the released glycans;

a cooling coil (152) arranged downstream of the reaction coil and adapted to receive the mixture from the reaction coil, the cooling coil configured to reduce a temperature of the mixture;

a glycan-binding column (124) fluidly coupled to the cooling coil and to the multi-port valve via a second port of the multi-port valve, the glycan-binding column configured to bind substantially all of the labeled glycans, the glycan-binding column adapted to receive an elution buffer solution via the second port of the multi-port valve, wherein the elution buffer solution elutes bound labeled glycans and carries the eluted labeled glycans to a glycan analysis device downstream of the glycan-binding column.

11. The system of claim 10, wherein:

the vessel comprises a bioreactor; and/or

the system further comprises a vacuum apparatus (150) arranged upstream of the reaction coil and downstream of the polypeptide-binding column and the first pump, the vacuum apparatus configured to substantially remove gas bubbles from the mixture comprising the glycan labeling reagent and the released glycan; and/or

the system further comprises a mixing chamber (157) arranged downstream of the polypeptide-binding column and upstream of the reaction coil, wherein the mixing chamber facilitates an adjustment of an elution buffer component of the labeled glycans to match a starting chromatographic mobile phase condition; and/or

the multi-port valve comprises a 12 satellite port and a central shared port valve; and/or

the polypeptide-binding column is selected from the group consisting of a protein A column, a protein G column, a protein A/G column, a protein L column, an amino acid column, an avidin column, a streptavidin column, a carbohydrate bonding column, a carbohydrate column, a glutathione column, a heparin column, a hydrophobic interaction column, an immunoaffinity column, a nucleotide/coenzyme column, a specialty column, and an immobilized-metal affinity chromatography (IMAC) column; and/or

wherein the glucanases are selected from the group consisting of endoglycosidases, glycosamidases, and O-glycanases, and combinations thereof; and/or

the glycan labelling reagent is a fluorophore or a chromophore.

12. The system of claim 11, wherein:

the endoglycosidases are selected from the group consisting of endoglycosidase D, endoglycosidase F (endoglycosidase F1, endoglycosidase F2, and

endoglycosidase F3 and combinations thereof), endoglycosidase H, endoglycosidase S, endoglycosidase M, and endoglycosidase B; or the glycosamidases are selected from the group consisting of glycopeptidases, peptide N-glycosidases, PNGases, N-glycohydrolases, and N-glycanases; or the O-glycanases are endo-GalNAc-ase D or endoGalNAc-ase A.

13. The system of claim 12, wherein the glycosamidases are selected from the group consisting of glycopeptidases, peptide N-glycosidases, PNGases, N-glycohydrolases, and N-glycanases and the PNGases is peptide:N-glycosidase F (PNGF).

14. The system of claim 11, wherein the glycan labelling reagent is a fluorophore or a chromophore and the fluorophore is selected from the group consisting of 2-aminobenzoic acid, 8-aminonaphthalene-1,3,6-trisulfonic acid disodium salt, 8-aminonaphthalene-1,3,6-trisulfonic acid trisodium salt, and anthranilamide, 4-methoxybenzamidine.

15. The system of claim 14, wherein the chromophore comprises 3-methyl-1-phenyl-2-pyrazoline-5-one or phenylhydrazine.

16. The system of any one of claims 10 to 15, wherein the glycan-binding column is a porous graphitic carbon column.

17. The system of any one of claims 10 to 16, further comprising:
a second pump (146) arranged upstream of the multi-port valve to pump the sample of the polypeptides from the vessel to the holding coil; and/or
a controller (132) communicatively coupled to the multi-port valve, the controller configured to selectively open and close the first and second ports of the multi-port valve; and/or

a heating element (232) positioned immediately adjacent the reaction coil, the heating element configured to maintain the reaction coil at a temperature of approximately 80 degrees Celsius.

18. A closed system for preparing a sample in real-time for glycan analysis, the closed system comprising:

- a multi-port valve (104);
- a holding coil (108) upstream of the multi-port valve;
- a polypeptide-binding column (112) fluidly coupled to and downstream of a first port of the multi-port valve;
- a reaction coil (120) arranged downstream of the polypeptide-binding column;
- a cooling coil (152) arranged downstream of the reaction coil;
- a glycan-binding column (124) fluidly coupled to and downstream of the cooling coil, the glycan-binding column fluidly coupled to the multi-port valve via a second port of the multi-port valve; and
- a controller (132) communicatively coupled to the multi-port valve and comprising a memory, a processor, and logic stored on the memory and executable by the processor to:
 - (a) move a sample of a product containing polypeptides to the holding coil;
 - (b) position the multi-port valve in a first position in which the holding coil is fluidly coupled to the polypeptide-binding column via the first port of the multi-port valve, such that the sample flows to the first column, whereby substantially all of the polypeptides in the sample bind to the polypeptide-binding column;
 - (c) when the multi-port valve is in the first position, move glucanases to the polypeptide-binding column via the holding coil to release glycans from the bound polypeptides, and then move a carrier solution to the polypeptide-binding column, via the holding coil, and through the polypeptide-binding column, thereby moving substantially all of the released glycans out of the polypeptide-binding column;
 - (d) move the released glycans toward the reaction coil;
 - (e) move a glycan-labeling reagent toward the released glycans prior to reaching the reaction coil, such that the glycan-labeling reagent mixes with the released glycans;

(f) move the mixture of the released glycans and the glycan-labeling reagent to the reaction coil, whereby the glycans in the mixture are labeled;

(g) move the mixture to a cooling coil arranged downstream of the reaction coil, wherein the cooling coil reduces a temperature of the mixture;

(h) move the mixture to the glycan-binding column, whereby the labeled glycans bind to the glycan-binding column;

(i) position the multi-port valve in a second position in which the glycan-binding column is fluidly coupled to a source of elution buffer solution via the second port of the multi-port valve; and

(j) when the multi-port valve is in the second position, move an elution buffer solution from the elution buffer solution source to the glycan-binding column, and through the glycan-binding column, thereby eluting glycans bound to the glycan-binding column.

19. The method or system of any one of the preceding claims, wherein the polypeptide is a therapeutic polypeptide and is selected from the group consisting of an antibody or antigen-binding fragment thereof, a derivative of an antibody or antibody fragment, and a fusion polypeptide.

20. The method or system of claim 19, wherein the antibody is selected from the group consisting of infliximab, bevacizumab, ranibizumab, cetuximab, ranibizumab, palivizumab, abagovomab, abciximab, actoxumab, adalimumab, afelimomab, afutuzumab, alacizumab, alacizumab pegol, ald518, alemtuzumab, alirocumab, alemtuzumab, altumomab, amatuximab, anatumomab mafenatox, anrukinzumab, apolizumab, arcitumomab, aselizumab, altinumab, atlizumab, atorolimumab, tocilizumab, bapineuzumab, basiliximab, bavituximab, bectumomab, belimumab, benralizumab, bertilimumab, besilesomab, bevacizumab, bezlotoxumab, biciromab, bivatazumab, bivatazumab mertansine, blinatumomab, blosozumab, brentuximab vedotin, briakinumab, brodalumab, canakinumab, cantuzumab mertansine, cantuzumab mertansine, caplacizumab, capromab pendetide, carlumab, catumaxomab, cc49, cedelizumab, certolizumab pegol, cetuximab, citatuzumab bogatox, cixutumumab,

clazakizumab, clenoliximab, clivatuzumab tetraxetan, conatumumab, crenezumab, cr6261, dacetuzumab, daclizumab, dalotuzumab, daratumumab, demcizumab, denosumab, detumomab, dorlimomab aritox, drozitumab, duligotumab, dupilumab, ecromeximab, eculizumab, edobacomab, edrecolomab, efalizumab, efungumab, elotuzumab, elsilimomab, enavatuzumab, enlimomab pegol, enokizumab, enokizumab, enoticumab, enoticumab, ensituximab, epitumomab cituxetan, epratuzumab, erlizumab, ertumaxomab, etaracizumab, etrolizumab, exbivirumab, exbivirumab, fanolesomab, faralimomab, farletuzumab, fasinumab, fbta05, felvizumab, fezakinumab, ficlatuzumab, figitumumab, flanvotumab, fontolizumab, foralumab, foravirumab, fresolimumab, fulranumab, futuximab, galiximab, ganitumab, gantenerumab, gavilimumab, gentuzumab ozogamicin, gevokizumab, girentuximab, glembatumumab vedotin, golimumab, gomiliximab, gs6624, ibalizumab, ibritumomab tiuxetan, icrucumab, igovomab, imciromab, imgatuzumab, inclacumab, indatuximab ravtansine, infliximab, intetumumab, inolimomab, inotuzumab ozogamicin, ipilimumab, iratumumab, itolizumab, ixekizumab, keliximab, labetuzumab, lebrikizumab, lemalesomab, lerdelimumab, lexatumumab, libivirumab, ligelizumab, lintuzumab, lirilumab, lorvotuzumab mertansine, lucatumumab, lumiliximab, mapatumumab, maslimomab, mavrilimumab, matuzumab, mepolizumab, metelimumab, milatuzumab, minretumomab, mitumomab, mogamulizumab, morolimumab, motavizumab, moxetumomab pasudotox, muromonab-cd3, nacolomab tafenatox, namilumab, naptumomab estafenatox, narnatumab, natalizumab, nebacumab, necitumumab, nerelimomab, nesvacumab, nimotuzumab, nivolumab, nofetumomab merpentan, ocaratuzumab, ocrelizumab, odulimumab, ofatumumab, olaratumab, olokizumab, omalizumab, onartuzumab, oportuzumab monatox, oregovomab, orticumab, otelixizumab, oxelumab, ozanezumab, ozoralizumab, pagibaximab, palivizumab, panitumumab, panobacumab, parsatuzumab, pascolizumab, pateclizumab, patritumab, pentumomab, perakizumab, pertuzumab, pexelizumab, pidilizumab, pintumomab, placulumab, ponezumab, priliximab, pritumumab, PRO 140, quilizumab, racotumomab, radretumab, rafivirumab, ramucirumab, ranibizumab, raxibacumab, regavirumab, reslizumab, rilotumumab, rituximab, robatumumab, roledumab, romosozumab, rontalizumab, rovelizumab, ruplizumab, samalizumab, sarilumab, satumomab pendetide, secukinumab, sevirumab,

sibrotuzumab, sifalimumab, siltuximab, simtuzumab, sipilizumab, sirukumab, solanezumab, solitomab, sonepcizumab, sontuzumab, stamulumab, sulesomab, suvizumab, tabalumab, tacatuzumab tetraxetan, tadocizumab, talizumab, tanezumab, taplitumomab paptox, tefibazumab, telimomab aritox, tenatumomab, tefibazumab, telimomab aritox, tenatumomab, teneliximab, teplizumab, teprotumumab, tezepelumab, TGN1412, tremelimumab, ticilimumab, tildrakizumab, tigatuzumab, TNX-650, tocilizumab, toralizumab, tositumomab, tralokinumab, trastuzumab, TRBS07, tregalizumab, tremelimumab, tucotuzumab celmoleukin, tuvirimab, ublituximab, urelumab, urtoxazumab, ustekinumab, vapaliximab, vatelizumab, vedolizumab, veltuzumab, vepalimomab, vesencumab, visilizumab, volociximab, vorsetuzumab mafodotin, votumumab, zalutumumab, zanolimumab, zatuximab, ziralimumab, zolimomab aritox, and those antibodies shown in Table 1; or wherein the therapeutic polypeptide is a polypeptide selected from the group consisting of a glycoprotein, CD polypeptide, a HER receptor polypeptide, a cell adhesion polypeptide, a growth factor polypeptide, an insulin polypeptide, an insulin-related polypeptide, a coagulation polypeptide, a coagulation-related polypeptide, albumin, IgE, a blood group antigen, a colony stimulating factor, a receptor, a neurotrophic factor, an interferon, an interleukin, a viral antigen, a lipoprotein, calcitonin, glucagon, atrial natriuretic factor, lung surfactant, tumor necrosis factor-alpha and -beta, enkephalinase, mouse gonadotropin-associated peptide, DNase, inhibin, activating, an integrin, protein A, protein D, a rheumatoid factor, an immunotoxin, a bone morphogenetic protein, a superoxide dismutase, a surface membrane polypeptide, a decay accelerating factor, an AIDS envelope, a transport polypeptide, a homing receptor, an addressin, a regulatory polypeptide, an immunoadhesin, a myostatin, a TALL polypeptide, an amyloid polypeptide, a thymic stromal lymphopoietin, a RANK ligand, a c-kit polypeptide, a TNF receptor, and an angiopoietin, and biologically active fragments, analogs or variants thereof.