

As such, there remains a need for alternative methods of reducing HCPs in the purification process of therapeutic or diagnostic proteins. Such alternative methods reduce HCPs preferably without affecting product stability, yield, or cost to ultimately maintain product quality and is amenable to large scale manufacturing and ensuring patient safety.

Summary

In one aspect of the present disclosure, there is provided a pharmaceutical composition comprising an antibody that binds to human N3pGlu A β (anti-N3pGlu A β antibody), wherein the anti-N3pGlu A β antibody was prepared by a process comprising purifying the anti-N3pGlu antibody from a mammalian host cell, and wherein the total content of host cell proteins (HCPs) in the composition is less than about 100 ppm (as measured by LCMS) and the composition comprises one of, combinations of, or all of the following host cell proteins: protein S100-A6, protein S100-A11, phospholipase B-like 2 protein, lysosomal protective protein, ubiquitin-40S ribosomal protein S27a, kallikrein-11, serine protease HTRA1 isoform X1, complement C1r subcomponent, actin, aortic smooth muscle isoform X1, heat shock cognate 71 kDa protein, and peroxiredoxin-1.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising an antibody that binds to human N3pGlu A β (anti-N3pGlu A β antibody), wherein the anti-N3pGlu A β antibody was prepared by a process comprising purifying the anti-N3pGlu antibody from a mammalian host cell, and wherein the total content of host cell proteins (HCPs) in the composition is less than about 10 ppm (as measured by LCMS) and the composition comprises one of, combinations of, or all of the following host cell proteins: polyubiquitin, lysosomal protective protein, glutathione S-transferase Y1, 40S ribosomal protein S28, thioredoxin isoform X1, basement membrane-specific heparan sulfate proteoglycan core protein isoform X1, tubulointerstitial nephritis antigen-like protein, actin – partial cytoplasmic 2 isoform X2, galectin-1, peroxiredoxin-1, and cornifin alpha.

Description

Accordingly, the present invention addresses one or more of the above problems by providing alternative methods of reducing HCPs in the preparation of therapeutic or diagnostic antibodies or antigen-binding fragments thereof. The methods of the present

invention provide reproducible methods that are highly effective in removing HCPs, whilst preserving antibody stability, reducing aggregation, maintaining product yield and have a potential to lower immunogenicity risk. Such methods can effectively remove HCPs without requiring increased antibody preparation volume. Surprisingly, the

5 methods of the present invention achieved HCP counts well below the industry acceptable standards of < 100 ppm. Surprisingly, other embodiments of the present invention achieved HCP counts of < 50 ppm whilst preserving protein stability, reducing aggregation, and maintaining product yield. More surprisingly, other embodiments of the present invention achieved HCP counts of < 20 ppm, < 10 ppm, < 5 ppm, < 1 ppm, or ~ 0
10 ppm, whilst preserving protein stability, reducing aggregation, and maintaining product yield. Furthermore, embodiments of the present invention provide methods of HCP removal that are applicable to a broad range of molecules. Other embodiments of the present invention enable the elimination of additional purification steps, resulting in a reduction in batch processing time, and decreased manufacturing costs. The disclosed
15 methods may be performed in order to produce antibody compositions having reduced host cell content, wherein the host cell content of the antibody compositions is less < 100 ppm, < 50 ppm, < 10 ppm, < 5 ppm, < 1 ppm, or ~ 0 ppm.

Accordingly, there is provided methods of reducing host cell protein content in an anti-N3pGlu A β antibody ("an anti-N3pG antibody") preparation. In some embodiments,
20 the anti-N3pG antibody is recombinantly produced in a mammalian host cell, such as a Chinese hamster ovary cell host cell.

Accordingly, in particular embodiments, provided is a method of reducing host cell protein content in a protein preparation comprising an anti-N3pG antibody

Claims

1. ~~A method of reducing host cell protein content in a protein preparation comprising an anti-N3pGlu A β antibody recombinantly produced in a mammalian host cell, the method comprising the steps of:~~
 - a. ~~subjecting the protein preparation to an affinity chromatography column;~~
 - b. ~~eluting the anti-N3pGlu A β antibody from the chromatography column with a combination of acids comprising of a weak acid and a strong acid to obtain an eluate comprising the anti-N3pGlu A β antibody;~~
 - c. ~~raising pH of the eluate to above about pH 5.0; and~~
 - d. ~~subjecting the eluate to a depth filter and obtaining a filtered protein preparation.~~
2. ~~The method of Claim 1, wherein the chromatography column comprises a Protein A, Protein G or Protein L affinity chromatography column.~~
3. ~~The method of Claim 1, wherein the weak acid and the strong acid is a monovalent acid up to about pH 7.3.~~
4. ~~The method of Claim 1, wherein the weak acid is acetic acid and the strong acid is phosphoric acid or lactic acid.~~
5. ~~The method of claim 4, wherein the concentration of the acetic acid is about 20 mM, and wherein the strong acid is phosphoric acid and wherein the concentration of the phosphoric acid is about 5 mM to about 10 mM.~~
6. ~~The method of Claim 4, wherein the concentration of the acetic acid is about 20 mM, and wherein the strong acid is lactic acid and wherein the concentration of the lactic acid is about 5 mM.~~
7. ~~The method of Claim 1, further comprising a step of performing viral inactivation.~~
8. ~~The method of Claim 1, further comprising a step of performing viral inactivation, comprising adjusting the pH of the eluate from said step of eluting the protein from the chromatography column, to below about pH 4.0, and wherein the eluate is maintained at below about pH 4.0 for about 0 minutes to about 180 minutes.~~
9. ~~The method of claim 8, wherein said step of adjusting the pH of the eluate comprises adjusting the pH of the eluate to about pH 3.3 to about pH 3.7~~
10. ~~The method of claim 9, wherein the pH of the eluate is adjusted to about pH 3.5.~~

- ~~11. The method of any one of claim 8 to 10, wherein adjusting the pH of the eluate comprises adding any one of HCl, phosphoric acid, or a combination of acetic acid and phosphoric acid.~~
- ~~12. The method of claim 1, wherein said step of raising the pH of the eluate comprises raising the pH to about pH 6.5 to about pH 7.5.~~
- ~~13. The method of claim 12, wherein the pH of the eluate is raised to about pH 7.0.~~
- ~~14. The method of any one of claim 12 or 13, wherein the step of raising the pH of the eluate comprises adding Tris.~~
- ~~15. The method of any one of claims 1 to 14, wherein the eluate at said step of raising the pH to above about 5.0 has an ionic strength of about 10 mM to about 45 mM.~~
- ~~16. The method of any one of claims 1 to 15, further comprising subjecting the depth filtered protein preparation to one of more of the following purification and/or polishing steps to obtain a drug substance preparation comprising an anti-N3pGlu A β antibody: viral inactivation, ion exchange chromatography, viral filtration, tangential flow filtration.~~
- ~~17. The method of any one of claims 1 to 16, wherein the depth filter is a cellulose/diatomaceous earth-based filter.~~
- ~~18. The method of claim 17, wherein the depth filter is B1HC filter, a X0HC filter, or a Zeta Plus (ZB Media) filter.~~
- ~~19. The method of any one of claims 1 to 16, wherein the depth filter is a synthetic filter.~~
- ~~20. The method of claim 19, wherein the depth filter is a C0SP filter, a X0SP filter, or a Emphaze AEX Hybrid Purifier filter.~~
- ~~21. The method of claim 20, wherein the depth filter is a X0SP filter.~~
- ~~22. The method of any one of claims 17-21, wherein the depth filter pore size is at least from about 9 μ to about 0.1 μ .~~
- ~~23. The method of claim 22, wherein the depth filter pore size is at least from about 2 μ to about 0.1 μ .~~
- ~~24. The method of claim 23, wherein the depth filter pore size is about 0.1 μ .~~
- ~~25. The method of any one of claims 1-24, wherein the pH of the eluate on the depth filter is about 5.0.~~

26. The method of any one of claims 1-24, wherein the pH of the eluate on the depth filter is about 6.0.
27. The method of any one of claims 1-24, wherein the pH of the eluate on the depth filter is about 7.0.
28. The method of any one of claims 1-27, wherein the mammalian cell is a CHO cell.
29. The method of any one of claims 1 to 28, wherein the protein preparation comprises a harvested cell culture fluid, a capture pool, or a recovered protein pool.
30. The method of any one of claims 1 to 29, wherein the anti-N3pGlu A β antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, a human antibody, a bispecific antibody, or an antibody fragment.
31. The method of Claim 30, wherein the anti-N3pGlu A β antibody is an IgG1 antibody.
32. The method of any one of claims 1 to 31, wherein the anti-N3pGlu A β antibody comprises a heavy chain (HC) and a light chain (LC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is KSSQSLLYSRGKTYLN (SEQ ID NO:17), LCDR2 is AVSKLDS (SEQ ID NO:18), LCDR3 is VQGTHYPFT (SEQ ID NO:19), HCDR1 is GYDFTRYIN (SEQ ID NO:20), HCDR2 is WINPGSGNTKYNEKFKG (SEQ ID NO:21), and HCDR3 is EGITVY (SEQ ID NO:22).
33. The method of claim 32, wherein the LC of the anti-N3pGlu A β antibody comprises a LCVR and the HC of the anti-N3pGlu A β antibody comprises a HCVR, wherein the LCVR is DIVMTQTPLSLSVTPGQPASISCKSSQSLLYSRGKTYLNWLLQKPGQSPQLLIY AVSKLD SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCVQGTHYPFTFGQG TKLEIK (SEQ ID NO:13) and the HCVR is QVQLVQSGAEVKKPGSSVKVSKASGYDFTRYINWVRQAPGQGLEWMGW INPGSGNTKYNEKFKGRVTITADESTSTAYMELSSLRSEDTAVYYCAREGITV YWGQGTTVTVSS (SEQ ID NO: 14).

34. The method of claim 32 or claim 33, wherein the LC of the anti-N3pGlu A β antibody is

DIVMTQTPLSLSVTPGQPASISCKSSQSLLYSRGKTYLNLWLLQKPGQSPQLLIY
AVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCVQGTHYPFTFGQG
TKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL
QSGNSQESVTEQDSKDSSTLSLTLSKADYEKHKVYACEVTHQGLSSPVT
KSFNRGEC (SEQ ID NO: 15) and the HC of the anti-N3pGlu A β antibody is
QVQLVQSGAEVKKPGSSVKVSKKASGYDFTRYINWVRQAPGQGLEWMGW
INPGSGNTKYNEKFKGRVTITADESTSTAYMELSSLRSEDTAVYYCAREGITV
YWGGQTTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 16).

35. The method of claim 34, wherein the anti-N3pGlu A β antibody is donanemab.

36. The method of any one of claims 32 to 35, wherein the host cell protein content in the filtered protein preparation is less than 100 ppm (as measured by LCMS).

37. The method of any one of claims 32-36, wherein the filtered protein preparation comprises one, combinations of, or all of the following host cell proteins: protein S100-A6, protein S100-A11, phospholipase B-like 2 protein, lysosomal protective protein, ubiquitin-40S ribosomal protein S27a, kallikrein-11, serine protease HTRA1 isoform X1, complement C1r subcomponent, actin, aortic smooth muscle isoform X1, heat shock cognate 71 kDa protein, and peroxiredoxin-1.

38. The method of claim 37, wherein the filtered protein preparation comprises less than about 5 ppm of protein S100-A6 (as measured by LCMS).

39. The method of claim 37 or claim 38, wherein the filtered protein preparation comprises less than about 5 ppm of protein S100-A11 (as measured by LCMS).

40. ~~The method of any one of claims 37-39, wherein the filtered protein preparation comprises less than about 10 ppm of phospholipase B-like 2 protein (as measured by LCMS).~~
41. ~~The method of any one of claims 37-40, wherein the filtered protein preparation comprises less than about 5 ppm of lysosomal protective protein (as measured by LCMS).~~
42. ~~The method of any one of claims 37-41, wherein the filtered protein preparation comprises less than about 5ppm of ubiquitin-40S ribosomal protein S27a (as measured by LCMS).~~
43. ~~The method of any one of claims 37-42, wherein the filtered protein preparation comprises less than about 5 ppm of kallikrein-11 (as measured by LCMS).~~
44. ~~The method of any one of claims 37-43, wherein the filtered protein preparation comprises less than about 5 ppm serine protease HTRA1 isoform X1 (as measured by LCMS).~~
45. ~~The method of any one of claims 37-44, wherein the filtered protein preparation comprises less than about 5 ppm complement C1r subcomponent (as measured by LCMS).~~
46. ~~The method of any one of claims 37-45, wherein the filtered protein preparation comprises less than about 5 ppm actin, aortic smooth muscle isoform X1 (as measured by LCMS).~~
47. ~~The method of any one of claims 37-46, wherein the filtered protein preparation comprises less than about 5 ppm actin, aortic smooth muscle isoform X1 (as measured by LCMS).~~
48. ~~The method of any one of claims 37-47, wherein the filtered protein preparation comprises less than about 5 ppm heat shock cognate 71 kDa protein (as measured by LCMS).~~
49. ~~The method of any one of claims 37-48, wherein the filtered protein preparation comprises less than about 5 ppm peroxiredoxin-1 (as measured by LCMS).~~
50. ~~The method of any one of claims 32 to 35, wherein the host cell protein content in the drug substance preparation is less than 100 ppm (as measured by LCMS).~~

51. The method of any one of claims 32-35 and 50, wherein the drug substance preparation comprises one of, combinations of, or all of the following host cell proteins: protein S100-A6, protein S100-A11, phospholipase B-like 2 protein, lysosomal protective protein, ubiquitin-40S ribosomal protein S27a, kallikrein-11, serine protease HTRA1 isoform X1, complement C1r subcomponent, actin, aortic smooth muscle isoform X1, heat shock cognate 71 kDa protein, and peroxiredoxin-1.
52. The method of claim 51, wherein the drug substance preparation comprises less than about 5 ppm of protein S100-A6 (as measured by LCMS).
53. The method of claim 51 or claim 52, wherein the drug substance preparation comprises less than about 5 ppm of protein S100-A11 (as measured by LCMS).
54. The method of any one of claims 51-53, wherein the drug substance preparation comprises less than about 10 ppm of phospholipase B-like 2 protein (as measured by LCMS).
55. The method of any one of claims 51-54, wherein the drug substance preparation comprises less than about 5 ppm of lysosomal protective protein (as measured by LCMS).
56. The method of any one of claims 51-55, wherein the drug substance preparation comprises less than about 5 ppm of ubiquitin-40S ribosomal protein S27a (as measured by LCMS).
57. The method of any one of claims 51-56, wherein the drug substance preparation comprises less than about 5 ppm of kallikrein-11 (as measured by LCMS).
58. The method of any one of claims 51-57, wherein the drug substance preparation comprises less than about 5 ppm serine protease HTRA1 isoform X1 (as measured by LCMS).
59. The method of any one of claims 51-58, wherein the drug substance preparation comprises less than about 5 ppm complement C1r subcomponent (as measured by LCMS).
60. The method of any one of claims 51-59, wherein the drug substance preparation comprises less than about 5 ppm actin, aortic smooth muscle isoform X1 (as measured by LCMS).

61. The method of any one of claims 51-60, wherein the drug substance preparation comprises less than about 5 ppm actin, aortic smooth muscle isoform X1 (as measured by LCMS).
62. The method of any one of claims 51-61, wherein the drug substance preparation comprises less than about 5 ppm heat shock cognate 71 kDa protein (as measured by LCMS).
63. The method of any one of claims 51-62, wherein the drug substance preparation comprises less than about 5 ppm peroxiredoxin 1 (as measured by LCMS).
64. The method of any one of claims 1-31, wherein the anti-N3pGlu A β antibody comprises a heavy chain (HC) and a light chain (LC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is RASQSLGNWLA (SEQ ID NO: 27), LCDR2 is YQASTLES (SEQ ID NO: 28), LCDR3 is QHYKGSFWT (SEQ ID NO: 29), HCDR1 is AASGFTFSSYPMS (SEQ ID NO: 30), HCDR2 is AISGSGGSTYYADSVKG (SEQ ID NO: 31), and HCDR3 is AREGGSGSYNGFDY (SEQ ID NO: 32).
65. The method of claim 64, wherein the LC of the anti-N3pGlu A β antibody comprises a LCVR and the HC of the anti-N3pGlu A β antibody comprises a HCVR, wherein the LCVR is
DIQMTQSPSTLSASVGDRVTITCRASQSLGNWLAWYQQKPGKAPKLLIYQAS
TLESGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQHYKGSFWTFGQGCTKVEI
K (SEQ ID NO: 23) and the HCVR is
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYPMSWVRQAPGKGLEWVSAIS
GSGGSTYYADSVKGRTISRDN SKNTLYLQMNSLRAEDTAVYYCAREGGSGS
YNGFDYWGQGTLVTVSS (SEQ ID NO: 24).
66. The method of claim 64 or claim 65, wherein the LC of the anti-N3pGlu A β antibody is
DIQMTQSPSTLSASVGDRVTITCRASQSLGNWLAWYQQKPGKAPKLLIYQAS
TLESGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQHYKGSFWTFGQGCTKVEI

KRTVAAPSVFIFPPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN
SQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR
GEC (SEQ ID NO: 25) and the HC of the anti-N3pGlu A β antibody is
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYPMSWVRQAPGKGLEWVSAIS
GSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAREGGSGS
YYNGFDYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNH
KPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVD
KSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPG (SEQ ID NO: 26).

67. The method of any one of claims 64 to 66, wherein the host cell protein content in the filtered protein preparation is less than 10 ppm (as measured by LCMS).
68. The method of any one of claims 64 to 67, wherein the filtered protein preparation comprises one of, combinations of, or all of the following host cell proteins: polyubiquitin, lysosomal protective protein, glutathione S-transferase Y1, 40S ribosomal protein S28, thioredoxin isoform X1, basement membrane-specific heparan sulfate proteoglycan core protein isoform X1, tubulointerstitial nephritis antigen-like protein, actin—partial cytoplasmic 2 isoform X2, galectin-1, peroxiredoxin-1, and cornifin alpha.
69. The method of claim 68, wherein the filtered protein preparation comprises less than about 1 ppm of polyubiquitin (as measured by LCMS).
70. The method of claim 68 or 69, wherein the filtered protein preparation comprises less than about 1 ppm of lysosomal protective protein (as measured by LCMS).
71. The method of any one of claims 68-70, wherein the filtered protein preparation comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).
72. The method of any one of claims 68-71, wherein the filtered protein comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).

73. ~~The method of any one of claims 68-72, wherein the filtered protein preparation comprises less than about 1 ppm of 40S ribosomal protein S28 (as measured by LCMS).~~
74. ~~The method of any one of claims 68-73, wherein the filtered protein preparation comprises less than about 1 ppm of thioredoxin isoform X1 (as measured by LCMS).~~
75. ~~The method of any one of claims 68-74, wherein the filtered protein preparation comprises less than about 1 ppm of basement membrane-specific heparan sulfate proteoglycan core protein isoform X1 (as measured by LCMS).~~
76. ~~The method of any one of claims 68-75, wherein the filtered protein preparation comprises less than about 1 ppm of tubulointerstitial nephritis antigen-like protein (as measured by LCMS).~~
77. ~~The method of any one of claims 68-76 wherein the filtered protein preparation comprises less than about 1 ppm of actin—partial cytoplasmic 2 isoform X2 (as measured by LCMS).~~
78. ~~The method of any one of claims 68-77, wherein the filtered protein preparation comprises less than about 1 ppm of galectin-1 (as measured by LCMS).~~
79. ~~The method of any one of claims 68-78, wherein the filtered protein preparation comprises less than about 1 ppm of peroxiredoxin-1 (as measured by LCMS).~~
80. ~~The method of any one of claims 68-79, wherein the filtered protein preparation comprises less than about 1 ppm of cornifin alpha (as measured by LCMS).~~
81. ~~The method of any one of claims 64-66, wherein the host cell protein content in the drug substance preparation is less than 10 ppm (as measured by LCMS).~~
82. ~~The method of any one of claims 64-66 and 81, wherein the drug substance preparation comprises one of, combinations of, or all of the following host cell proteins: polyubiquitin, lysosomal protective protein, glutathione S-transferase Y1, 40S ribosomal protein S28, thioredoxin isoform X1, basement membrane-specific heparan sulfate proteoglycan core protein isoform X1, tubulointerstitial nephritis antigen-like protein, actin—partial cytoplasmic 2 isoform X2, galectin-1, peroxiredoxin-1, and cornifin alpha.~~
83. ~~The method of claim 82, wherein the drug substance preparation comprises less than about 1 ppm of polyubiquitin (as measured by LCMS).~~

84. The method of claim 82 or 83, wherein the drug substance preparation comprises less than about 1 ppm of lysosomal protective protein (as measured by LCMS).
85. The method of any one of claims 82-84, wherein the drug substance preparation comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).
86. The method of any one of claims 82-85, wherein the drug substance comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).
87. The method of any one of claims 82-86, wherein the drug substance preparation comprises less than about 1 ppm of 40S ribosomal protein S28 (as measured by LCMS).
88. The method of any one of claims 82-87, wherein the drug substance preparation comprises less than about 1 ppm of thioredoxin isoform X1 (as measured by LCMS).
89. The method of any one of claims 82-88, wherein the drug substance preparation comprises less than about 1 ppm of basement membrane-specific heparan sulfate proteoglycan core protein isoform X1 (as measured by LCMS).
90. The method of any one of claims 82-89, wherein the drug substance preparation comprises less than about 1 ppm of tubulointerstitial nephritis antigen-like protein (as measured by LCMS).
91. The method of any one of claims 82-90 wherein the drug substance preparation comprises less than about 1 ppm of actin—partial cytoplasmic 2 isoform X2 (as measured by LCMS).
92. The method of any one of claims 82-91, wherein the drug substance preparation comprises less than about 1 ppm of galectin-1 (as measured by LCMS).
93. The method of any one of claims 82-92, wherein the drug substance preparation comprises less than about 1 ppm of peroxiredoxin-1 (as measured by LCMS).
94. The method of any one of claims 82-93, wherein the drug substance preparation comprises less than about 1 ppm of cornifin alpha (as measured by LCMS).
95. A composition produced by the method of any one of claims 1-94.
96. A method of reducing host cell protein content in a protein preparation comprising an anti-N3pGlu A β antibody recombinantly produced in a mammalian host cell, the method comprising the steps of:

- ~~a) subjecting the protein preparation to an affinity chromatography column;~~
- ~~b) eluting the anti-N3pGlu A β antibody from the chromatography column to obtain an eluate comprising the anti-N3pGlu A β antibody;~~
- ~~c) adjusting, if necessary, the pH of the eluate to between pH 5.0 and pH 7.5, subjecting the eluate to a depth filter and obtaining a filtered protein preparation, wherein the depth filter is a fully synthetic depth filter.~~

~~97. The method of Claim 96, wherein the chromatography column comprises a Protein A, Protein G or Protein L affinity chromatography column.~~

~~98. The method of Claim 96 or 97, wherein the depth filter pore size is at least from about 9 μ to about 0.1 μ .~~

~~99. The method of claim 98, wherein the depth filter pore size is at least from about 2 μ to about 0.1 μ .~~

~~100.—The method of claim 99, wherein the depth filter pore size is about 0.1 μ .~~

~~101.—The method of any one of claims 96–100, wherein the depth filter is a X0SP filter.~~

~~102.—The method of any one of claims 96–101, wherein the pH of the eluate on the depth filter is about 5.0.~~

~~103.—The method of any one of claims 96–101, wherein the pH of the eluate on the depth filter is about 6.0.~~

~~104.—The method of any one of claims 96–101, wherein the pH of the eluate on the depth filter is about 7.0.~~

~~105.—The method of any one of claims 96–104, wherein the mammalian cell is a CHO cell.~~

~~106.—The method of any one of claims 96–105, wherein the protein preparation comprises a harvested cell culture fluid, a capture pool, or a recovered protein pool.~~

~~107.—The method of any one of claims 96 to 106, wherein the anti-N3pGlu A β antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, a human antibody, a bispecific antibody, or an antibody fragment.~~

~~108.—The method of Claim 107, wherein the anti-N3pGlu A β antibody is an IgG1 antibody.~~

~~109.—The method of any one of claims 96 to 108, wherein the anti-N3pGlu A β antibody comprises a heavy chain (HC) and a light chain (LC), wherein the light chain~~

comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences L~~CDR1~~, L~~CDR2~~, and L~~CDR3~~, and the HCVR comprises amino acid sequences H~~CDR1~~, H~~CDR2~~, and H~~CDR3~~, wherein L~~CDR1~~ is KSSQSLLYSRGKTYLN (SEQ ID NO:17), L~~CDR2~~ is AVSKLDS (SEQ ID NO:18), L~~CDR3~~ is VQGTHYPFT (SEQ ID NO:19), H~~CDR1~~ is GYDFTRYIN (SEQ ID NO:20), H~~CDR2~~ is WINPGSGNTKYNEKFKG (SEQ ID NO:21), and H~~CDR3~~ is EGITVY (SEQ ID NO:22).

110.—The method of claim 109, wherein the LC of the anti-N3pGlu A β antibody comprises a LCVR and the HC of the anti-N3pGlu A β antibody comprises a HCVR, wherein the LCVR is DIVMTQTPLSLSVTPGQPASISCKSSQSLLYSRGKTYLNWLLQKPGQSPQLLIY AVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCVQGTHYPFTFGQG TKLEIK (SEQ ID NO:13) and the HCVR is QVQLVQSGAEVKKPGSSVKVSKASGYDFTRYINWVRQAPGQGLEWMGW INPGSGNTKYNEKFKGRVTITADESTSTAYMELSSLRSED~~TA~~VYYCAREGITV YWGQGT~~TV~~TVSS (SEQ ID NO: 14).

111.—The method of claim 109 or claim 110, wherein the LC of the anti-N3pGlu A β antibody is DIVMTQTPLSLSVTPGQPASISCKSSQSLLYSRGKTYLNWLLQKPGQSPQLLIY AVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCVQGTHYPFTFGQG TKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL QSGNSQESVTEQDSKDS~~TY~~SLSS~~TL~~TL~~SK~~ADYEKHKVYACEVTHQGLSSPVT KSFNRGEC (SEQ ID NO: 15) and the HC of the anti-N3pGlu A β antibody is QVQLVQSGAEVKKPGSSVKVSKASGYDFTRYINWVRQAPGQGLEWMGW INPGSGNTKYNEKFKGRVTITADESTSTAYMELSSLRSED~~TA~~VYYCAREGITV YWGQGT~~TV~~TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSV~~TV~~PS~~SL~~GTQTYICNVNHKPSNTK VDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNKKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT

CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ
QGNVFCSSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 16).

- 112.—The method of claim 111, wherein the anti-N3pGlu A β antibody is donanemab.
- 113.—The method of any one of claims 109 to 112, wherein the host cell protein content in the filtered protein preparation is less than 100 ppm (as measured by LCMS).
- 114.—The method of any one of claims 109-113, wherein the filtered protein preparation comprises one, combinations of, or all of the following host cell proteins: protein S100-A6, protein S100-A11, phospholipase B-like 2 protein, lysosomal protective protein, ubiquitin-40S ribosomal protein S27a, kallikrein-11, serine protease HTRA1 isoform X1, complement C1r subcomponent, actin, aortic smooth muscle isoform X1, heat shock cognate 71 kDa protein, and peroxiredoxin-1.
- 115.—The method of claim 114, wherein the filtered protein preparation comprises less than about 5 ppm of protein S100-A6 (as measured by LCMS).
- 116.—The method of claim 114 or claim 115, wherein the filtered protein preparation comprises less than about 5 ppm of protein S100-A11 (as measured by LCMS).
- 117.—The method of any one of claims 114-116, wherein the filtered protein preparation comprises less than about 10 ppm of phospholipase B-like 2 protein (as measured by LCMS).
- 118.—The method of any one of claims 114-117 wherein the filtered protein preparation comprises less than about 5 ppm of lysosomal protective protein (as measured by LCMS).
- 119.—The method of any one of claims 114-118, wherein the filtered protein preparation comprises less than about 5ppm of ubiquitin-40S ribosomal protein S27a (as measured by LCMS).
- 120.—The method of any one of claims 114-119, wherein the filtered protein preparation comprises less than about 5 ppm of kallikrein-11 (as measured by LCMS).
- 121.—The method of any one of claims 114-120, wherein the filtered protein preparation comprises less than about 5 ppm serine protease HTRA1 isoform X1 (as measured by LCMS).

- 122.—~~The method of any one of claims 114-121, wherein the filtered protein preparation comprises less than about 5 ppm complement C1r subcomponent (as measured by LCMS).~~
- 123.—~~The method of any one of claims 114-122, wherein the filtered protein preparation comprises less than about 5 ppm actin, aortic smooth muscle isoform X1 (as measured by LCMS).~~
- 124.—~~The method of any one of claims 114-123, wherein the filtered protein preparation comprises less than about 5 ppm actin, aortic smooth muscle isoform X1 (as measured by LCMS).~~
- 125.—~~The method of any one of claims 114-124, wherein the filtered protein preparation comprises less than about 5 ppm heat shock cognate 71 kDa protein (as measured by LCMS).~~
- 126.—~~The method of any one of claims 114-125, wherein the filtered protein preparation comprises less than about 5 ppm peroxiredoxin-1 (as measured by LCMS).~~
- 127.—~~The method of any one of claims 109-112, wherein the host cell protein content in the drug substance preparation is less than 100 ppm (as measured by LCMS).~~
- 128.—~~The method of any one of claims 109-112 and 127, wherein the drug substance preparation comprises one of, combinations of, or all of the following host cell proteins: protein S100-A6, protein S100-A11, phospholipase B-like 2 protein, lysosomal protective protein, ubiquitin-40S ribosomal protein S27a, kallikrein-11, serine protease HTRA1 isoform X1, complement C1r subcomponent, actin, aortic smooth muscle isoform X1, heat shock cognate 71 kDa protein, peroxiredoxin-1.~~
- 129.—~~The method of claim 128, wherein the drug substance preparation comprises less than about 5 ppm of protein S100-A6 (as measured by LCMS).~~
- 130.—~~The method of claim 128 or claim 129, wherein the drug substance preparation comprises less than about 5 ppm of protein S100-A11 (as measured by LCMS).~~
- 131.—~~The method of any one of claims 128-130, wherein the drug substance preparation comprises less than about 10 ppm of phospholipase B-like 2 protein (as measured by LCMS).~~

- 132.—~~The method of any one of claims 128–131, wherein the drug substance preparation comprises less than about 5 ppm of lysosomal protective protein (as measured by LCMS).~~
- 133.—~~The method of any one of claims 128–132, wherein the drug substance preparation comprises less than about 5ppm of ubiquitin–40S ribosomal protein S27a (as measured by LCMS).~~
- 134.—~~The method of any one of claims 128–133, wherein the drug substance preparation comprises less than about 5 ppm of kallikrein–11 (as measured by LCMS).~~
- 135.—~~The method of any one of claims 128–134, wherein the drug substance preparation comprises less than about 5 ppm serine protease HTRA1 isoform X1 (as measured by LCMS).~~
- 136.—~~The method of any one of claims 128–135, wherein the drug substance preparation comprises less than about 5 ppm complement C1r subcomponent (as measured by LCMS).~~
- 137.—~~The method of any one of claims 128–136, wherein the drug substance preparation comprises less than about 5 ppm actin, aortic smooth muscle isoform X1 (as measured by LCMS).~~
- 138.—~~The method of any one of claims 128–137, wherein the drug substance preparation comprises less than about 5 ppm actin, aortic smooth muscle isoform X1 (as measured by LCMS).~~
- 139.—~~The method of any one of claims 128–138, wherein the drug substance preparation comprises less than about 5 ppm heat shock cognate 71 kDa protein (as measured by LCMS).~~
- 140.—~~The method of any one of claims 128–139, wherein the drug substance preparation comprises less than about 5 ppm peroxiredoxin–1 (as measured by LCMS).~~
- 141.—~~The method of any one of claims 96 to 108, wherein the anti–N3pGlu–A β antibody comprises a heavy chain (HC) and a light chain (LC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LC1DR1, LC1DR2, and LC1DR3, and the HCVR comprises amino acid sequences HC1DR1, HC1DR2, and HC1DR3, wherein LC1DR1 is RASQSLGNWLA~~

(SEQ ID NO: 27), LCDR2 is YQASTLES (SEQ ID NO: 28). LCDR3 is QHYKGSFWT (SEQ ID NO: 29), HCDR1 is AASGFTFSSYPMS (SEQ ID NO: 30), HCDR2 is AISGSGGSTYYADSVKG (SEQ ID NO: 31), and HCDR3 is AREGGSGSYNGFDY (SEQ ID NO: 32).

142.—The method of claim 141, wherein the LC of the anti-N3pGlu A β antibody comprises a LCVR and the HC of the anti-N3pGlu A β antibody comprises a HCVR, wherein the LCVR is DIQMTQSPSTLSASVGDRVTITCRASQSLGNWLAWYQQKPGKAPKLLIYQAS TLESGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQHYKGSFWTFGQGTKVEIK (SEQ ID NO:23) and the HCVR is EVQLLES GGGLVQPGGSLRLSCAASGFTFSSYPMSWVRQAPGKGLEWVSAIS GSGGSTYYADSVKGRTISRDN SKNTLYLQMNSLRAEDTAVYYCAREGGSGSYNGFDYWGQGTLVTVSS (SEQ ID NO: 24).

143.—The method of claim 141 or claim 142, wherein the LC of the anti-N3pGlu A β antibody is DIQMTQSPSTLSASVGDRVTITCRASQSLGNWLAWYQQKPGKAPKLLIYQAS TLESGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQHYKGSFWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 25) and the HC of the anti-N3pGlu A β antibody is EVQLLES GGGLVQPGGSLRLSCAASGFTFSSYPMSWVRQAPGKGLEWVSAIS GSGGSTYYADSVKGRTISRDN SKNTLYLQMNSLRAEDTAVYYCAREGGSGSYNGFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 26).

144.—The method of any one of claims 141-143, wherein the host cell protein content in the filtered protein preparation is less than 10 ppm (as measured by LCMS).

- 145.—~~The method of any one of claims 141–144, wherein the filtered protein preparation comprises one of, combinations of, or all of the following host cell proteins: polyubiquitin, lysosomal protective protein, glutathione S-transferase Y1, 40S ribosomal protein S28, thioredoxin isoform X1, basement membrane-specific heparan sulfate proteoglycan core protein isoform X1, tubulointerstitial nephritis antigen-like protein, actin—partial cytoplasmic 2 isoform X2, galectin-1, peroxiredoxin-1, and cornifin alpha.~~
- 146.—~~The method of claim 145, wherein the filtered protein preparation comprises less than about 1 ppm of polyubiquitin (as measured by LCMS).~~
- 147.—~~The method of claim 145 or 146, wherein the filtered protein preparation comprises less than about 1 ppm of lysosomal protective protein (as measured by LCMS).~~
- 148.—~~The method of any one of claims 145–147, wherein the filtered protein preparation comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).~~
- 149.—~~The method of any one of claims 145–148, wherein the composition comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).~~
- 150.—~~The method of any one of claims 145–149, wherein the filtered protein preparation comprises less than about 1 ppm of 40S ribosomal protein S28 (as measured by LCMS).~~
- 151.—~~The method of any one of claims 145–150, wherein the filtered protein preparation comprises less than about 1 ppm of thioredoxin isoform X1 (as measured by LCMS).~~
- 152.—~~The method of any one of claims 145–151, wherein the filtered protein preparation comprises less than about 1 ppm of basement membrane-specific heparan sulfate proteoglycan core protein isoform X1 (as measured by LCMS).~~
- 153.—~~The method of any one of claims 145–152, wherein the filtered protein preparation comprises less than about 1 ppm of tubulointerstitial nephritis antigen-like protein (as measured by LCMS).~~
- 154.—~~The method of any one of claims 145–153, wherein the filtered protein preparation comprises less than about 1 ppm of actin—partial cytoplasmic 2 isoform X2 (as measured by LCMS).~~

- 155.—~~The method of any one of claims 145–154, wherein the filtered protein preparation comprises less than about 1 ppm of galectin-1 (as measured by LCMS).~~
- 156.—~~The method of any one of claims 145–155, wherein the filtered protein preparation comprises less than about 1 ppm of peroxiredoxin-1 (as measured by LCMS).~~
- 157.—~~The method of any one of claims 145–156, wherein the filtered protein preparation comprises less than about 1 ppm of cornifin alpha (as measured by LCMS).~~
- 158.—~~The method of any one of claims 141–143, wherein the host cell protein content in the drug substance preparation is less than 10 ppm (as measured by LCMS).~~
- 159.—~~The method of any one of claims 141–143 and 158, wherein the drug substance preparation comprises one of, combinations of, or all of the following host cell proteins: polyubiquitin, lysosomal protective protein, glutathione S-transferase Y1, 40S ribosomal protein S28, thioredoxin isoform X1, basement membrane-specific heparan sulfate proteoglycan core protein isoform X1, tubulointerstitial nephritis antigen-like protein, actin—partial cytoplasmic 2 isoform X2, galectin-1, peroxiredoxin-1, and cornifin alpha.~~
- 160.—~~The method of claim 159, wherein the drug substance preparation comprises less than about 1 ppm of polyubiquitin (as measured by LCMS).~~
- 161.—~~The method of claim 158 or 160, wherein the drug substance preparation comprises less than about 1 ppm of lysosomal protective protein (as measured by LCMS).~~
- 162.—~~The method of any one of claims 158–161, wherein the drug substance preparation comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).~~
- 163.—~~The method of any one of claims 158–162, wherein the drug substance comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).~~
- 164.—~~The method of any one of claims 158–163, wherein the drug substance preparation comprises less than about 1 ppm of 40S ribosomal protein S28 (as measured by LCMS).~~
- 165.—~~The method of any one of claims 158–164, wherein the drug substance preparation comprises less than about 1 ppm of thioredoxin isoform X1 (as measured by LCMS).~~

- ~~166.—The method of any one of claims 158–165, wherein the drug substance preparation comprises less than about 1 ppm of basement membrane-specific heparan sulfate proteoglycan core protein isoform X1 (as measured by LCMS).~~
- ~~167.—The method of any one of claims 158–166, wherein the drug substance preparation comprises less than about 1 ppm of tubulointerstitial nephritis antigen-like protein (as measured by LCMS).~~
- ~~168.—The method of any one of claims 158–167 wherein the drug substance preparation comprises less than about 1 ppm of actin—partial cytoplasmic 2 isoform X2 (as measured by LCMS).~~
- ~~169.—The method of any one of claims 158–168, wherein the drug substance preparation comprises less than about 1 ppm of galectin 1 (as measured by LCMS).~~
- ~~170.—The method of any one of claims 158–169, wherein the drug substance preparation comprises less than about 1 ppm of peroxiredoxin 1 (as measured by LCMS).~~
- ~~171.—The method of any one of claims 158–170, wherein the drug substance preparation comprises less than about 1 ppm of cornifin alpha (as measured by LCMS).~~
- ~~172.—A composition produced by the method of any one of claims 96–171.~~
- ~~173.1.~~ A pharmaceutical composition comprising an antibody that binds to human N3pGlu A β (anti-N3pGlu A β antibody), wherein the anti-N3pGlu A β antibody was prepared by a process comprising purifying the anti-N3pGlu antibody from a mammalian host cell, and wherein the total content of host cell proteins (HCPs) in the composition is less than about 100 ppm (as measured by LCMS) and the composition comprises one of, combinations of, or all of the following host cell proteins: protein S100-A6, protein S100-A11, phospholipase B-like 2 protein, lysosomal protective protein, ubiquitin-40S ribosomal protein S27a, kallikrein-11, serine protease HTRA1 isoform X1, complement C1r subcomponent, actin, aortic smooth muscle isoform X1, heat shock cognate 71 kDa protein, and peroxiredoxin-1.
- ~~174.2.~~ A pharmaceutical composition according to claim ~~173~~1, wherein the mammalian cell is a CHO cell.
- ~~175.3.~~ A pharmaceutical composition according to claim ~~173~~1 or claim ~~174~~2, wherein the anti-N3pGlu A β antibody is a monoclonal antibody, a chimeric antibody, a

humanized antibody, a human antibody, a bispecific antibody, or an antibody fragment.

176.4. A pharmaceutical composition according to claim 1753, wherein the anti-N3pGlu A β antibody is an IgG1 antibody.

177.5. A pharmaceutical composition according to ~~any one of~~ claims ~~173-1761~~, wherein the anti-N3pGlu A β antibody comprises a heavy chain (HC) and a light chain (LC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is KSSQSLLYSRGKTYLN (SEQ ID NO:17), LCDR2 is AVSKLDS (SEQ ID NO:18), LCDR3 is VQGTHYPFT (SEQ ID NO:19), HCDR1 is GYDFTRYIN (SEQ ID NO:20), HCDR2 is WINPGSGNTKYNEKFKG (SEQ ID NO:21), and HCDR3 is EGITVY (SEQ ID NO:22).

178.6. A pharmaceutical composition according to claim 1771, wherein the LC of the anti-N3pGlu A β antibody comprises a LCVR and the HC of the anti-N3pGlu A β antibody comprises a HCVR, wherein the LCVR is DIVMTQTPLSLSVTPGQPASISCKSSQSLLYSRGKTYLNWLLQKPGQSPQLLIY AVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCVQGTHYPFTFGQG TKLEIK (SEQ ID NO:13) and the HCVR is QVQLVQSGAEVKKPGSSVKVSKASGYDFTRYINWVRQAPGQGLEWMGW INPGSGNTKYNEKFKGRVTITADESTSTAYMELSSLRSEDTAVYYCAREGITV YWGQGTTVTVSS (SEQ ID NO: 14).

179.7. A pharmaceutical composition according claim ~~177 or claim 1781~~, wherein the LC of the anti-N3pGlu A β antibody is DIVMTQTPLSLSVTPGQPASISCKSSQSLLYSRGKTYLNWLLQKPGQSPQLLIY AVSKLDSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCVQGTHYPFTFGQG TKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL QSGNSQESVTEQDSKSTYSLSTLTLSKADYEEKHKVYACEVTHQGLSSPVT KSFNRGEC (SEQ ID NO: 15) and the HC of the anti-N3pGlu A β antibody is QVQLVQSGAEVKKPGSSVKVSKASGYDFTRYINWVRQAPGQGLEWMGW

INPGSGNTKYNEKFKGRVTITADESTSTAYMELSSLRSED TAVYYCAREGITV
YWGQGTTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS
WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV
VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDS DGSFFLYSKLTVDKSRWQ
QGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 16).

~~180.8.~~ A pharmaceutical composition according to claim ~~179~~1, wherein the anti-N3pGlu A β antibody is donanemab.

~~181.~~ ~~A pharmaceutical composition according to any one of claims 173-180, wherein the composition comprises one of, combinations of, or all of the following host cell proteins: protein S100-A6, protein S100-A11, phospholipase B-like 2 protein, lysosomal protective protein, ubiquitin-40S ribosomal protein S27a, kallikrein-11, serine protease HTRA1 isoform X1, complement C1r subcomponent, actin, aortic smooth muscle isoform X1, heat shock cognate 71 kDa protein, and peroxiredoxin 1.~~

~~182.9.~~ A pharmaceutical composition according to claim ~~181~~1, wherein the composition comprises less than about 5 ppm of protein S100-A6 (as measured by LCMS).

~~183.10.~~ ~~_____~~ A pharmaceutical composition according to claim ~~181 or claim 182~~1, wherein the composition comprises less than about 5 ppm of protein S100-A11 (as measured by LCMS).

~~184.11.~~ ~~_____~~ A pharmaceutical composition according to ~~claim 1 any one of claims 181-183~~claim 1, wherein the composition comprises less than about 10 ppm of phospholipase B-like 2 protein (as measured by LCMS).

~~185.12.~~ ~~_____~~ A pharmaceutical composition according to ~~claim 1 any one of claims 181-184~~claim 1, wherein the composition comprises less than about 5 ppm of lysosomal protective protein (as measured by LCMS).

~~186.13.~~ ~~_____~~ A pharmaceutical composition according to ~~claim 1 any one of claims 181-185~~claim 1, wherein the composition comprises less than about 5ppm of ubiquitin-40S ribosomal protein S27a (as measured by LCMS).

- ~~187.14.~~ 14. A pharmaceutical composition according to claim 1~~any one of claims 181-186~~, wherein the composition comprises less than about 5 ppm of kallikrein-11 (as measured by LCMS).
- ~~188.15.~~ 15. A pharmaceutical composition according to claim 1~~any one of claims 181-187~~, wherein the composition comprises less than about 5 ppm serine protease HTRA1 isoform X1 (as measured by LCMS).
- ~~189.16.~~ 16. A pharmaceutical composition according to claim 1~~any one of claims 181-188~~, wherein the composition comprises less than about 5 ppm complement C1r subcomponent (as measured by LCMS).
- ~~190.17.~~ 17. A pharmaceutical composition according to claim 1~~any one of claims 181-189~~, wherein the composition comprises less than about 5 ppm actin,~~aortic smooth muscle isoform X1~~ (as measured by LCMS).
- ~~191.18.~~ 18. A pharmaceutical composition according to claim 1~~any one of claims 181-190~~, wherein the composition comprises less than about 5 ppm ~~actin~~, aortic smooth muscle isoform X1 (as measured by LCMS).
- ~~192.19.~~ 19. A pharmaceutical composition according to claim 1~~any one of claims 181-191~~, wherein the composition comprises less than about 5 ppm heat shock cognate 71 kDa protein (as measured by LCMS).
- ~~193.20.~~ 20. A pharmaceutical composition according to claim 1~~any one of claims 181-192~~, wherein the composition comprises less than about 5 ppm peroxiredoxin-1 (as measured by LCMS).
- ~~194.~~ 21. The pharmaceutical composition according to ~~any one of claims 173-176~~, wherein the anti-N3pGlu A β antibody comprises a heavy chain (HC) and a light chain (LC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1, HCDR2, and HCDR3, wherein LCDR1 is RASQSLGNWLA (SEQ ID NO: 27), LCDR2 is YQASTLES (SEQ ID NO: 28), LCDR3 is QHYKGSFWT (SEQ ID NO: 29), HCDR1 is AASGFTFSSYPMS (SEQ ID NO: 30), HCDR2 is AISGSGGSTYYADSVKG (SEQ ID NO: 31), and HCDR3 is AREGGSGSYNGFDY (SEQ ID NO: 32).

195.—The pharmaceutical composition of claim 194, wherein the LC of the anti-N3pGlu A β antibody comprises a LCVR and the HC of the anti-N3pGlu A β antibody comprises a HCVR, wherein the LCVR is
DIQMTQSPSTLSASVGDRVTITCRASQSLGNWLAWYQQKPGKAPKLLIYQAS
TLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYKGSFWTFGQGTKVEI
K (SEQ ID NO: 23) and the HCVR is
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYPMSWVRQAPGKGLEWVSAIS
GSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAREGGSGS
YYNGFDYWGQGT LVT VSS (SEQ ID NO: 24);

196.—The pharmaceutical composition of claim 194 or claim 195, wherein the LC of the anti-N3pGlu A β antibody is
DIQMTQSPSTLSASVGDRVTITCRASQSLGNWLAWYQQKPGKAPKLLIYQAS
TLESGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQHYKGSFWTFGQGTKVEI
KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN
SQESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR
GEG (SEQ ID NO: 25) and the HC of the anti-N3pGlu A β antibody is
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYPMSWVRQAPGKGLEWVSAIS
GSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAREGGSGS
YYNGFDYWGQGT LVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP
EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNH
KPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV
LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD
KSRWQQGNV FSC SVMHEALHNHYTQKSLSLSPG (SEQ ID NO: 26);

197.21. A pharmaceutical composition comprising an antibody that binds to human N3pGlu A β (anti-N3pGlu A β antibody), wherein the anti-N3pGlu A β antibody was prepared by a process comprising purifying the anti-N3pGlu antibody from a mammalian host cell, and wherein the total content of host cell proteins (HCPs) in the composition is less than about 10 ppm (as measured by LCMS) and the composition comprises one of, combinations of, or all of the following host cell proteins:

polyubiquitin, lysosomal protective protein, glutathione S-transferase Y1, 40S ribosomal protein S28, thioredoxin isoform X1, basement membrane-specific heparan sulfate proteoglycan core protein isoform X1, tubulointerstitial nephritis antigen-like protein, actin – partial cytoplasmic 2 isoform X2, galectin-1, peroxiredoxin-1, and cornifin alpha according to any one of claims 194-196, wherein the total content of host cell proteins (HCPs) in the composition is less than about 10 ppm (as measured by LCMS).

~~198. — A pharmaceutical composition according to claim 197, wherein the composition comprises one, combinations of, or all of the following host cell proteins: polyubiquitin, lysosomal protective protein, glutathione S-transferase Y1, 40S ribosomal protein S28, thioredoxin isoform X1, basement membrane-specific heparan sulfate proteoglycan core protein isoform X1, tubulointerstitial nephritis antigen-like protein, actin – partial cytoplasmic 2 isoform X2, galectin-1, peroxiredoxin-1, and cornifin alpha.~~

~~199.~~22. — A pharmaceutical composition according to claim ~~21~~198, wherein the composition comprises less than about 1 ppm of polyubiquitin (as measured by LCMS).

~~200.~~23. — A pharmaceutical composition according to claim ~~21~~198 ~~or 199~~, wherein the composition comprises less than about 1 ppm of lysosomal protective protein (as measured by LCMS).

~~201.~~24. — A pharmaceutical composition according to claim 21 ~~any one of claims 198-200~~, wherein the composition comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).

~~202. — A pharmaceutical composition according to any one of claims 198-201, wherein the composition comprises less than about 1 ppm of glutathione S-transferase Y1 (as measured by LCMS).~~

~~203.~~25. — A pharmaceutical composition according to claim 21 ~~any one of claims 198-202~~, wherein the composition comprises less than about 1 ppm of 40S ribosomal protein S28 (as measured by LCMS).

~~204-26.~~ A pharmaceutical composition according to ~~claim 21~~~~any one of claims 198-203~~, wherein the composition comprises less than about 1 ppm of thioredoxin isoform X1 (as measured by LCMS).

~~205-27.~~ A pharmaceutical composition according to ~~claim 21~~~~any one of claims 198-204~~, wherein the composition comprises less than about 1 ppm of basement membrane-specific heparan sulfate proteoglycan core protein isoform X1 (as measured by LCMS).

~~206-28.~~ A pharmaceutical composition according to ~~claim 21~~~~any one of claims 198-205~~, wherein the composition comprises less than about 1 ppm of tubulointerstitial nephritis antigen-like protein (as measured by LCMS).

~~207-29.~~ A pharmaceutical composition according to ~~claim 21~~~~any one of claims 198-206~~, wherein the composition comprises less than about 1 ppm of actin – partial cytoplasmic 2 isoform X2 (as measured by LCMS).

~~208-30.~~ A pharmaceutical composition according to ~~claim 21~~~~any one of claims 198-207~~, wherein the composition comprises less than about 1 ppm of galectin-1 (as measured by LCMS).

~~209-31.~~ A pharmaceutical composition according to ~~claim 21~~~~any one of claims 198-208~~, wherein the composition comprises less than about 1 ppm of peroxiredoxin-1 (as measured by LCMS).

~~32.~~ A pharmaceutical composition according to claim 21, wherein the mammalian cell is a CHO cell.

~~33.~~ A pharmaceutical composition according to claim 21, wherein the anti-N3pGlu A β antibody is a monoclonal antibody, a chimeric antibody, a humanized antibody, a human antibody, a bispecific antibody, or an antibody fragment.

~~34.~~ A pharmaceutical composition according to claim 33, wherein the anti-N3pGlu A β antibody is an IgG1 antibody.

~~35.~~ The pharmaceutical composition according to claim 21, wherein the anti-N3pGlu A β antibody comprises a heavy chain (HC) and a light chain (LC), wherein the light chain comprises a light chain variable region (LCVR) and the heavy chain comprises a heavy chain variable region (HCVR), wherein the LCVR comprises amino acid sequences LCDR1, LCDR2, and LCDR3, and the HCVR comprises amino acid sequences HCDR1,

HCDR2, and HCDR3, wherein LCDR1 is RASQSLGNWLA (SEQ ID NO: 27), LCDR2 is YQASTLES (SEQ ID NO: 28). LCDR3 is QHYKGSFWT (SEQ ID NO: 29), HCDR1 is AASGFTFSSYPMS (SEQ ID NO: 30), HCDR2 is AISGSGGSTYYADSVKG (SEQ ID NO: 31), and HCDR3 is AREGGSGSYNGFDY (SEQ ID NO: 32).

36. The pharmaceutical composition of claim 21, wherein the LC of the anti-N3pGlu A β antibody comprises a LCVR and the HC of the anti-N3pGlu A β antibody comprises a HCVR, wherein the LCVR is

DIQMTQSPSTLSASVGDRVTITCRASQSLGNWLAWYQQKPGKAPKLLIYQASTLE SGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQHYKGSFWTFGQGTKVEIK (SEQ ID NO:23) and the HCVR is

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYPMSWVRQAPGKGLEWVSAISGS GGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAREGGSGSYN GFDYWGQGT LVT VSS (SEQ ID NO: 24).

37. The pharmaceutical composition of claim 21, wherein the LC of the anti-N3pGlu A β antibody is

DIQMTQSPSTLSASVGDRVTITCRASQSLGNWLAWYQQKPGKAPKLLIYQASTLE SGVPSRFSGSGSGTEFTLTISLQPDDEFATYYCQHYKGSFWTFGQGTKVEIKRTVA APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQ DSKDSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 25) and the HC of the anti-N3pGlu A β antibody is

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYPMSWVRQAPGKGLEWVSAISGS GGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAREGGSGSYN GFDYWGQGT LVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVD KKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYK CKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHE ALHNHYTQKSLSLSPG (SEQ ID NO: 26).