METHODS OF REDUCING THE ENZYMATIC HYDROLYSIS ACTIVITY RATE IN A COMPOSITION OBTAINED FROM A PURIFICATION PLATFORM

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority benefit to U.S. Provisional Patent Application No. 62/961,609, filed on January 15, 2020, and U.S. Provisional Patent Application No. 62/843,261, filed on May 3, 2019, the disclosure of each of which is hereby incorporated by reference in its entirety.

TECHNICAL FIELD

[0002] The present disclosure provides purification platforms comprising a depth filtration step and/or a hydrophobic interaction chromatography (HIC) step. Also disclosed herein are methods of using the purification platforms described herein and compositions obtained therefrom.

BACKGROUND

[0003] Biotherapeutic products, such as antibodies, produced from host cell cultures require purification to remove host cell proteins and other impurities that may impact, *e.g.*, product quality and therapeutic efficacy. Current purification methods may not remove all host cell proteins and impurities, including host cell hydrolytic enzymes. Host cell proteins and impurities remaining with the purification target can thus impact the purification target itself as well as other additives, *e.g.*, components added for formulation purposes, such as surfactants. Accordingly, there is a need for improved methods for purifying biotherapeutic products produced from host cell cultures for pharmaceutical use.

[0004] All references cited herein, including patent applications and publications, are incorporated by reference in their entirety.

SUMMARY

[0005] In one ~~aspect~~example, the present disclosure refers to a method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: (a) a capture step; and (b) a depth filtration step, thereby

reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0005a] In one aspect, the present disclosure refers to a method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step; and (b) a depth filtration step, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite, thereby reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0006] In some examples, the enzymatic hydrolysis activity rate is an enzymatic polysorbate hydrolysis activity rate. In some examples, the relative reduction of the enzymatic hydrolysis activity rate of the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 20%.

[0006a] In one aspect, the present disclosure refers to a method of reducing the level of one or more hydrolytic enzymes in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step; and (b) a depth filtration step, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite, thereby reducing the level of the hydrolytic enzyme in the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0007] In another ~~aspect~~example, the present disclosure refers to a method of reducing the level of one or more hydrolytic enzymes in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: (a) a capture step; and (b) a depth filtration step, thereby reducing the level of the hydrolytic enzyme in the composition as compared to purification of the sample using the same purification platform without the depth filtration step. In some examples, the one or more hydrolytic enzymes are capable of hydrolyzing a polysorbate. In some examples, the relative reduction of the level of one or more hydrolytic enzymes in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 20%.

[0007a] In one aspect, the present disclosure refers to a method for reducing degradation of a polysorbate in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step; and (b) a depth filtration step, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite, thereby reducing degradation of the polysorbate in the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0008] In another ~~aspect~~example, the present disclosure refers to a method for reducing degradation of a polysorbate in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising: (a) a capture step; and (b) a depth filtration step, thereby reducing degradation of the polysorbate in the composition as compared to purification of the sample using the same purification platform without the depth filtration step. In some examples, the relative reduction of degradation of the polysorbate in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 5%.

[0009] In some examples, the purification platform is for purification of a target from the sample, wherein the sample comprises the target and one or more host cell impurities. In some examples, the target comprises a polypeptide. In some examples, the host cell impurity is a host cell protein.

[0010] In some examples, the depth filtration step is performed prior to the capture step, or the depth filtration step is performed after the capture step.

[0017] In some examples, the purification platform further comprises a hydrophobic interaction chromatography (HIC) purification step. In some examples, the HIC purification step is performed prior to, in between, or after the one or more purification steps, if present. In some examples, the HIC purification step is performed after the one or more purification steps and prior to the UFDF step, if present.

[0018] In some examples, the purification platform further comprises a pH hold step, wherein the pH hold step is performed after the one or more purification steps, if present, and prior to the UFDF step.

[0019] In some examples, the purification platform further comprises a virus filtration step, wherein the virus filtration step is performed after the pH hold step and prior to the UFDF step. In some examples, the virus filtration step comprises processing via a virus filter.

[0020] In some examples, the HIC purification step comprises processing via a HIC filter.

[0021] In some examples, the one or more purification steps each independently comprise processing via a chromatography selected from the group consisting of: ion exchange chromatography, anion exchange chromatography, cation exchange chromatography, a hydrophobic charge induction chromatography, a ceramic hydroxyapatite chromatography, and a multimodal chromatography. In some examples, the one or more purification steps each independently comprise processing via a chromatography selected from the group consisting of: DEAE, DMAE, TMAE, QAE, SPSFF, SPXL, QSFF, MEP-Hypercel™, Capto MMC, and Capto Adhere.

[0021a] In one aspect, the present disclosure refers to a method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step comprising processing via affinity chromatography; (b) a virus inactivation step; (c) a depth filtration step; (d) a second polypeptide purification step; (e) a third polypeptide purification step; and (f) a ultrafiltration/diafiltration (UFDF) step, wherein the depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite, thereby reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0022] In another ~~aspect~~example, the present disclosure refers to a method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a capture step comprising processing via affinity chromatography; (b) a virus inactivation step; (c) a second polypeptide purification step; (d) a third polypeptide purification step; and (e) a ultrafiltration/diafiltration (UFDF) step, wherein the purification platform further comprises a depth filtration step performed at one or more of the following: (i) prior to the capture step; (ii) after the capture step and prior to the virus inactivation step; (iii) after the virus inactivation step and prior to the second polypeptide purification step; (iv) after the second polypeptide purification step and prior to the third polypeptide purification step; or (v) after the third polypeptide purification step and prior to the ultrafiltration/diafiltration (UFDF) step; thereby reducing the enzymatic hydrolysis activity rate of

the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

[0023] In some examples, the purification platform further comprises, in the following order, a pH hold step and a virus filtration step performed after the third polypeptide purification step and prior to the UFDF step. In some examples, the virus filtration step comprises processing via a virus filter.

[0024] In some examples, the purification platform further comprises a hydrophobic interaction chromatography (HIC) purification step performed at one or more of the following: (i) after the third polypeptide purification step and prior to the pH hold step; (ii) after the pH hold step and prior to the virus filtration step; or (iii) after the virus filtration step and prior to the UFDF step.

[0024a] In one aspect, the present disclosure refers to a method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order: (a) a first depth filtration step; (b) a capture step comprising processing via affinity chromatography; (c) a virus inactivation step; and (d) a second depth filtration step; wherein the second depth filtration step comprises processing via a depth filter, and wherein the depth filter of the second depth filtration step comprises cellulose fibers, diatomaceous earth, and perlite, thereby reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the second depth filtration step.

[0025] In some examples, the method further comprises determining the enzymatic hydrolysis activity rate of the composition.

[0026] In some examples, the method further comprises determining the level of one or more hydrolytic enzymes in the composition.

[0027] In some examples, the composition comprises a polysorbate. In some examples, the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80.

[0028] In some examples, the method further comprises comprising a sample processing step.

[0029] In some examples, the sample is, or is derived from, a cell culture sample. In some examples, the cell culture sample comprises a host cell, and wherein the host cell is a Chinese hamster ovary (CHO) cell or an *E. coli* cell. In some examples, the sample comprises a host cell or components originating therefrom. In some examples, the sample comprises one or more host cell proteins, and wherein one of the one or more host cell proteins is a hydrolytic enzyme.

[0030] In some examples, the hydrolytic enzyme is a lipase, an esterase, a thioesterase, a phospholipase, or a ceramidase.

[0031] In some examples, the sample comprises a target, and wherein the target is an antibody moiety. In some examples, the antibody moiety is a monoclonal antibody. In some examples, the antibody moiety is a human, humanized, or chimeric antibody.

[0032] In some examples, the antibody moiety is selected from the group consisting of an anti-CD20 antibody, an anti-CD40 antibody, an anti-HER2 antibody, an anti-IL6 antibody, an anti-IgE antibody, an anti-IL13 antibody, an anti-TIGIT antibody, an anti-PD-L1 antibody, an anti-VEGF-A antibody, an anti-VEGF-A/ANG2 antibody, an anti-CD79b antibody, an anti-ST2 antibody, an anti-factor D antibody, an anti-factor IX antibody, an anti-factor X antibody, an anti-abeta antibody, an anti-tau antibody, an anti-CEA antibody, an anti-CEA/CD3 antibody, an anti-CD20/CD3 antibody, an anti-FcRH5/CD3 antibody, an anti-Her2/CD3 antibody, an anti-FGFR1/KLB antibody, a FAP-4-1 BBL fusion protein, a FAP-IL2v fusion protein, and a TYRP1 TCB antibody.

[0033] In some examples, the antibody moiety is selected from the group consisting of ocrelizumab, pertuzumab, trastuzumab, tocilizumab, faricimab, polatuzumab, gantenerumab, cibisatamab, crenezumab, mosunetuzumab, tiragolumab, bevacizumab, rituximab, atezolizumab, obinutuzumab, lampalizumab, lebrikizumab, omalizumab ranibizumab, emicizumab, selicrelumab, prasinezumab, RO6874281, and RO7122290.

[0034] In another example, provided is a pharmaceutical composition obtained from any one of the methods described herein.

~~**[0034a]** In one aspect, the present disclosure refers to a pharmaceutical composition obtained from the method disclosed herein.~~

[0035] In another example, provided is a formulated antibody moiety composition comprising a polysorbate, wherein the composition has a reduced polysorbate hydrolysis activity rate, and wherein the shelf-life of the composition is more than 24 months.

~~**[0035a]** In one aspect, the present disclosure refers to a formulated antibody moiety composition comprising an antibody moiety and a polysorbate wherein the composition has a reduced polysorbate hydrolysis activity rate, wherein the shelf-life of the composition is more than 24 months.~~

[0036] In another ~~aspect~~example, the present disclosure refers to a formulated antibody moiety composition comprising an antibody moiety and a polysorbate, wherein the composition has a reduced polysorbate hydrolysis activity rate, wherein the shelf-life of the composition is extended compared to the shelf-life indicated in documents filed with a health authority related to the formulated antibody moiety composition, wherein the shelf-life is extended by at least 6 months compared to the shelf-life indicated in said documents.

[0037] In another ~~aspect~~example, the present disclosure refers to a formulated antibody moiety composition comprising an antibody moiety, wherein the formulated antibody moiety composition has a reduced degradation of polysorbate, wherein the degradation is reduced by at least about 20% compared to the degradation indicated in documents filed with a health authority related to the formulated antibody moiety composition.

[0038] In another ~~aspect~~example, the present disclosure refers to a formulated antibody moiety composition comprising an antibody moiety and a polysorbate, wherein the polysorbate is degraded during storage of the liquid composition by 20% or less per year.

[0039] In some examples, the antibody moiety of a formulated antibody moiety composition is a monoclonal antibody. In some examples, the antibody moiety of a formulated antibody moiety composition is a human, humanized, or chimeric antibody.

[0040] In some examples, the antibody moiety of a formulated antibody moiety composition is selected from the group consisting of an anti-CD20 antibody, an anti-CD40 antibody, an anti-HER2 antibody, an anti-IL6 antibody, an anti-IgE antibody, an anti-IL13 antibody, an anti-TIGIT antibody, an anti-PD-L1 antibody, an anti-VEGF-A antibody, an anti-VEGF-A/ANG2 antibody, an anti-CD79b antibody, an anti-ST2 antibody, an anti-factor D antibody, an anti-factor IX antibody, an anti-factor X antibody, an anti-abeta antibody, an anti-tau antibody, an anti-CEA antibody, an anti-CEA/CD3 antibody, an anti-CD20/CD3 antibody, an anti-FcRH5/CD3 antibody, an anti-Her2/CD3 antibody, an anti-FGFR1/KLB antibody, a FAP-4-1 BBL fusion protein, a FAP-IL2v fusion protein, and a TYRP1 TCB antibody.

[0041] In some examples, the antibody moiety of a formulated antibody moiety composition is selected from the group consisting of ocrelizumab, pertuzumab, trastuzumab, tocilizumab, faricimab, polatuzumab, gantenerumab, cibisatamab, crenezumab, mosunetuzumab, tiragolumab, bevacizumab, rituximab, atezolizumab, obinutuzumab, lampalizumab, lebrikizumab, omalizumab ranibizumab, emicizumab, selicrelumab, prasinezumab, RO6874281, and RO7122290.

[0042] In some examples, the polysorbate hydrolysis activity rate of a formulated antibody moiety composition is reduced by at least about 20%. In some examples, the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80.

[0043] In another ~~aspect~~example, the present disclosure refers to a method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in order: (a) a capture step comprising processing via affinity chromatography; and (b) a purification step comprising processing via a chromatography selected from the group consisting of a HIC, a cation exchange chromatography, and a multimodal chromatography, wherein the purification platform further comprises one or more depth filtration

steps, wherein the one or more depth filtration steps are performed at any one or more of: prior to the capture step; after the capture step; or after the capture step and prior to the purification step, wherein each depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises materials selected from the group consisting of: (i) a silica and a polyacrylic fiber; (ii) a hydrogel Q (quaternary amine)-functionalized non-woven media and a multi-zone microporous membrane; and (iii) cellulose fibers, diatomaceous earth, and perlite, thereby reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the one or more depth filtration steps. In some examples, the enzymatic hydrolysis activity rate is an enzymatic polysorbate hydrolysis activity rate. In some examples, the relative reduction of the enzymatic hydrolysis activity rate of the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 20%.

[0044] In another ~~aspect~~example, the present disclosure refers to a method of reducing the level of one or more hydrolytic enzymes in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in order: (a) a capture step comprising processing via affinity chromatography; and (b) a purification step comprising processing via a chromatography selected from the group consisting of a HIC, a cation exchange chromatography, and a multimodal chromatography, wherein the purification platform further comprises one or more depth filtration steps, wherein the one or more depth filtration steps are performed at any one or more of: prior to the capture step; after the capture step and prior to the purification step; or after the purification step, wherein each depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises materials selected from the group consisting of: (i) a silica and a polyacrylic fiber; (ii) a hydrogel Q (quaternary amine)-functionalized non-woven media and a multi-zone microporous membrane; and (iii) cellulose fibers, diatomaceous earth, and perlite, thereby reducing the level of one or more hydrolytic enzymes in the composition as compared to purification of the sample using the same purification platform without the one or more depth filtration steps. In some examples, the one or more hydrolytic enzymes are capable of hydrolyzing a polysorbate. In some examples, the relative reduction of the level of one or more hydrolytic enzymes in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 20%.

[0045] In another ~~aspect~~example, the present disclosure refers to a method of reducing degradation of a polysorbate in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in order: (a) a capture step comprising processing via affinity chromatography; and (b) a purification step comprising processing via a chromatography selected from the group consisting of a HIC, a cation exchange chromatography, and a multimodal chromatography, wherein the purification platform further comprises one or more depth filtration steps, wherein the one or more depth filtration steps are performed at any one or more of: prior to the capture step; after the capture step; or after the capture step and prior to the purification step, wherein each depth filtration step comprises processing via a depth filter, and wherein the depth filter comprises materials selected from the group consisting of: (i) a silica and a polyacrylic fiber; (ii) a hydrogel Q (quaternary amine)-functionalized non-woven media and a multi-zone microporous membrane; and (iii) cellulose fibers, diatomaceous earth, and perlite, thereby reducing degradation of a polysorbate in the composition as compared to purification of the sample using the same purification platform without the one or more depth filtration steps. In some examples, the relative reduction of degradation of the polysorbate in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 5%.

[0046] In some examples, the depth filter comprising the silica and the polyacrylic fiber comprises a silica filter aid and a polyacrylic fiber pulp.

[0047] In some examples, depth filter comprising the hydrogel Q-functionalized non-woven media and the multi-zone microporous membrane comprises four layers comprising hydrogel Q-functionalized non-woven materials and a nine-zone microporous membrane.

[0048] In some examples, the depth filter comprising cellulose fibers, diatomaceous earth, and perlite comprises two layers, wherein each layer comprises a cellulose filter matrix, wherein the cellulose filter matrix is impregnated with a filter aid comprising one or more of diatomaceous earth or perlite, and wherein each layer further comprises a resin binder.

[0049] In some examples, the depth filter is selected based on the pH of the solution entering the depth filter. In some examples, the depth filter comprising the silica and the polyacrylic fiber is selected when the solution entering the depth filter is about 5 to about 6.5. In some examples, the depth filter comprising the hydrogel Q-functionalized non-woven media

from the group consisting of ocrelizumab, pertuzumab, trastuzumab, tocilizumab, faricimab, polatuzumab, gantenerumab, cibisatamab, crenezumab, mosunetuzumab, tiragolumab, bevacizumab, rituximab, atezolizumab, obinutuzumab, lampalizumab, lebrikizumab, omalizumab ranibizumab, emicizumab, selicrelumab, prasinezumab, RO6874281, and RO7122290.

[0065] In another example, provided is a pharmaceutical composition obtained from any of the methods described herein.

~~**[0065a]** In one aspect, the present disclosure refers to a pharmaceutical composition obtained from the method disclosed herein.~~

[0066] Those skilled in the art will recognize that several examples are possible within the scope and spirit of the disclosure of this application. The disclosure is illustrated further by the examples below, which are not to be construed as limiting the disclosure in scope or spirit to the specific procedures described therein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0067] **FIG. 1A** shows exemplary steps of a purification platform **100**. **FIG. 1B** shows exemplary options for steps of purification platforms.

[0068] **FIG. 2** shows a bar graph of the amount of free fatty acids measured in compositions obtained from purification platforms using a FAMS assay.

[0069] **FIG. 3** shows a bar graph of the hydrolytic activity measured in compositions obtained from purification platforms using a lipase activity assay.

[0070] **FIG. 4** shows a bar graph of the amount of free fatty acids measured in compositions obtained from purification platforms using a FAMS assay.

[0071] **FIG. 5** shows a schematic of purification options for faricimab.

[0072] **FIGS. 6A** and **6B** show bar graphs of PS20 hydrolytic activity measured in FcXL eluate for faricimab before (**FIG. 6A**) and after filtration on PDD1 filter (**FIG. 6B**).

[0073] **FIG. 7** shows a bar graph of the amount of free fatty acids measured in compositions obtained from purification platforms using a FAMS assay.

[0074] **FIGS. 8A-8B** show bar graphs of the hydrolytic activity measured in protein A eluates following filtration using a depth filter.

[0075] **FIG. 9** shows relative levels of CHOP and polysorbate degradation activity of protein A eluates following EMPHAZE™ depth filter clarification.

CLAIMS

What is claimed is:

1. A method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order:

   (a) a capture step; and

   (b) a depth filtration step,

   wherein the depth filtration step comprises processing via a depth filter, and

   wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite,

   thereby reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

2. The method of claim 1, wherein the enzymatic hydrolysis activity rate is an enzymatic polysorbate hydrolysis activity rate.

3. The method of claim 1 or 2, wherein the relative reduction of the enzymatic hydrolysis activity rate of the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least ~~about~~ 20%.

4. A method of reducing the level of one or more hydrolytic enzymes in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order:

   (a) a capture step; and

   (b) a depth filtration step,

   wherein the depth filtration step comprises processing via a depth filter, and

   wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite,

   thereby reducing the level of the hydrolytic enzyme in the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

5. The method of claim 4, wherein the one or more hydrolytic enzymes are capable of hydrolyzing a polysorbate.

6. The method of claim 4 or 5, wherein the relative reduction of the level of one or more hydrolytic enzymes in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least ~~about~~ 20%.

7. A method for reducing degradation of a polysorbate in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order:

(a) a capture step; and

(b) a depth filtration step,

wherein the depth filtration step comprises processing via a depth filter, and

wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite,

thereby reducing degradation of the polysorbate in the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

8. The method of claim 7, wherein the relative reduction of degradation of the polysorbate in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least ~~about~~ 5%.

9. The method of any one of claims 1-8, wherein the purification platform is for purification of a target from the sample, wherein the sample comprises the target and one or more host cell impurities.

10. The method of claim 9, wherein the target comprises a polypeptide.

11. The method of claim 9 or 10, wherein the host cell impurity is a host cell protein.

~~12. The method of any one of claims 1-11, wherein the depth filtration step is performed prior to the capture step, or the depth filtration step is performed after the capture step.~~

~~13. The method of any one of claims 1-12, wherein the depth filtration step comprises processing via a depth filter.~~

~~14. The method of claim 13, wherein the depth filter comprises a substrate comprising one or more of a diatomaceous earth composition, a silica composition, a cellulose fiber, a polymeric fiber, a cohesive resin, and an ash composition.~~

~~15. The method of claim 14, wherein at least a portion of the substrate of the depth filter comprises a surface modification.~~

~~16. The method of claim 15, wherein the surface modification is one or more of a quaternary amine surface modification, a cationic surface modification, and an anionic surface modification.~~

~~17. The method of any one of claims 14-16, wherein the depth filter is selected from the group consisting of an EMPHAZE™ depth filter, a PDD1 depth filter, a ZETA PLUS™ 120ZA depth filter, and a ZETA PLUS™ 120ZB depth filter.~~

~~18~~12. The method of any one of claims 1-~~17~~11, wherein the capture step comprises processing via affinity chromatography.

~~19~~13. The method of claim ~~18~~12, wherein the affinity chromatography is selected from the group consisting of a protein A chromatography, a protein G chromatography, a protein A/G chromatography, a protein L chromatography, a FcXL chromatography, a protein XL chromatography, a kappa chromatography, and a kappaXL chromatography.

~~20~~14. The method of any one of claims 1-~~19~~13, wherein the purification platform further comprises a virus inactivation step, wherein the virus inactivation step is performed after the capture step.

~~21~~15. The method of claim ~~20~~14, wherein the depth filtration step is performed after the virus inactivation step.

~~22~~16. The method of any one of claims 1-~~21~~15, wherein the purification platform further comprises a second ~~another~~ depth filtration step performed prior to the capture step.

17. The method of claim 16, wherein the second depth filtration step comprises processing via a second depth filter.

18. The method of claim 17, wherein the second depth filter comprises a substrate comprising one or more of a diatomaceous earth composition, a silica composition, a cellulose fiber, a polymeric fiber, a cohesive resin, and an ash composition.

19. The method of claim 18, wherein at least a portion of the substrate of the second depth filter comprises a surface modification.

20. The method of claim 19, wherein the surface modification is one or more of a quaternary amine surface modification, a cationic surface modification, and an anionic surface modification.

21. The method of any one of claims 1-20, wherein the purification platform further comprises a sterilization step performed prior to the capture step and, if present, after the second depth filtration step, wherein the sterilization step comprises processing via a sterile filter.

~~23~~22. The method of any one of claims 1-~~22~~21, wherein the purification platform further comprises one or more purification steps, and wherein the one or more purification steps is performed after the capture step, the depth filtration step, and, if present, the virus inactivation step.

~~24~~23. The method of claim ~~23~~22, wherein the one or more purification steps comprise polypeptide purification steps.

~~25~~24. The method of claim ~~23~~ 22 or ~~24~~23, wherein the purification platform further comprises another depth filtration step performed prior to, in between, or after the one or more purification steps.

~~26~~25. The method of any one of claims 1-~~25~~24, wherein the purification platform further comprises an ultrafiltration/diafiltration (UFDF) step, and wherein the UFDF step is performed after the one or more purification steps.

~~27~~26. The method of claim ~~26~~25, wherein the purification platform further comprises another depth filtration step performed prior to or after the UFDF step.

~~28~~27. The method of any one of claims 1-~~27~~26, wherein the purification platform further comprises a hydrophobic interaction chromatography (HIC) purification step.

~~29~~28. The method of claim ~~28~~27, wherein the HIC purification step is performed prior to, in between, or after the one or more purification steps, if present.

~~30~~29. The method of claim ~~28~~27, wherein the HIC purification step is performed after the one or more purification steps and prior to the UFDF step, if present.

~~31~~30. The method of claim ~~26~~ 25 or ~~27~~26, wherein the purification platform further comprises a pH hold step, wherein the pH hold step is performed after the one or more purification steps, if present, and prior to the UFDF step.

~~32~~31. The method of claim ~~31~~30, wherein the purification platform further comprises a virus filtration step, wherein the virus filtration step is performed after the pH hold step and prior to the UFDF step.

~~33~~32. The method of claim ~~32~~31, wherein the virus filtration step comprises processing via a virus filter.

~~34~~33. The method of claim ~~28~~27, wherein the HIC purification step comprises processing via a HIC filter.

~~35~~34. The method of any one of claims ~~23~~22-~~34~~33, wherein the one or more purification steps each independently comprise processing via a chromatography selected from the group consisting of: ion exchange chromatography, anion exchange chromatography, cation

exchange chromatography, a hydrophobic charge induction chromatography, a ceramic hydroxyapatite chromatography, and a multimodal chromatography.

~~36~~35. The method of any one of claims ~~23~~22-~~35~~34, wherein the one or more purification steps each independently comprise processing via a chromatography selected from the group consisting of: DEAE~~,~~; DMAE~~,~~; TMAE~~,~~; QAE~~,~~; crosslinked, beaded-form of agarose; quaternary amine, crosslinked, beaded-form of agarose; and mercaptoethylpyridine (MEP)~~SPSFF, SPXL, QSFF, MEP Hypercel™, Capto MMC, and Capto Adhere~~.

~~37~~36. A method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order:

(a) a capture step comprising processing via affinity chromatography;

(b) a virus inactivation step;

(c) a depth filtration step;

(~~c~~d) a second polypeptide purification step;

(~~d~~e) a third polypeptide purification step; and

(~~e~~f) a ultrafiltration/diafiltration (UFDF) step,

~~wherein the purification platform further comprises a depth filtration step performed at one or more of the following:~~

~~(i) prior to the capture step;~~

~~(ii) after the capture step and prior to the virus inactivation step;~~

~~(iii) after the virus inactivation step and prior to the second polypeptide purification step;~~

~~(iv) after the second polypeptide purification step and prior to the third polypeptide purification step; or~~

~~(v) after the third polypeptide purification step and prior to the ultrafiltration/diafiltration (UFDF) step;~~

wherein the depth filtration step comprises processing via a depth filter, and

wherein the depth filter comprises cellulose fibers, diatomaceous earth, and perlite,

thereby reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the depth filtration step.

~~38~~37. The method of claim ~~37~~36, wherein the purification platform further comprises, in the following order, a pH hold step and a virus filtration step performed after the third polypeptide purification step and prior to the UFDF step.

~~39~~38. The method of claim ~~38~~37, wherein the virus filtration step comprises processing via a virus filter.

~~40~~39. The method of any one of claims ~~37~~36-~~39~~38, wherein the purification platform further comprises a hydrophobic interaction chromatography (HIC) purification step performed at one or more of the following:

(i) after the third polypeptide purification step and prior to the pH hold step;

(ii) after the pH hold step and prior to the virus filtration step; or

(iii) after the virus filtration step and prior to the UFDF step.

40. A method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in the following order:

(a) a first depth filtration step;

(b) a capture step comprising processing via affinity chromatography;

(c) a virus inactivation step; and

(d) a second depth filtration step;

wherein the second depth filtration step comprises processing via a depth filter, and

wherein the depth filter of the second depth filtration step comprises cellulose fibers, diatomaceous earth, and perlite,

thereby reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the second depth filtration step.

41. The method of claim 40, wherein the first depth filtration step comprises processing via a depth filter.

42. The method of claim 41, wherein the depth filter of the first depth filtration step comprises a substrate comprising one or more of a diatomaceous earth composition, a silica composition, a cellulose fiber, a polymeric fiber, a cohesive resin, and an ash composition.

43. The method of claim 42, wherein at least a portion of the substrate of the depth filter of the first depth filtration step comprises a surface modification.

44. The method of claim 43, wherein the surface modification is one or more of a quaternary amine surface modification, a cationic surface modification, and an anionic surface modification.

45. The method of any one of claims 40-44, wherein the purification platform further comprises a sterilization step performed after the first depth filtration step and prior to the capture step, wherein the sterilization step comprises processing via a sterile filter.

46. The method of any one of claims 1-45, wherein the depth filter comprising cellulose fibers, diatomaceous earth, and perlite comprises two layers.

47. The method of claim 46, wherein each layer comprises a cellulose filter matrix, wherein the cellulose filter matrix is impregnated with a filter aid comprising one or more of diatomaceous earth or perlite, and wherein each layer further comprises a resin binder.

~~41~~48. The method of any one of claims 1-~~40~~47, further comprising determining the enzymatic hydrolysis activity rate of the composition.

~~42~~49. The method of any one of claims 1-~~41~~48, further comprising determining the level of one or more hydrolytic enzymes in the composition.

~~43~~50. The method of any one of claims 1-~~42~~49, wherein the composition comprises a polysorbate.

~~44~~51. The method of claim ~~43~~50, wherein the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80.

~~45~~52. The method of any one of claims 1-~~44~~51, further comprising a sample processing step.

~~46~~53. The method of any one of claims 1-~~45~~52, wherein the sample is, or is derived from, a cell culture sample.

~~47~~54. The method of claim ~~46~~53, wherein the cell culture sample comprises a host cell, and wherein the host cell is a Chinese hamster ovary (CHO) cell or an *E. coli* cell.

~~48~~55. The method of any one of claims 1-~~47~~54, wherein the sample comprises a host cell or components originating therefrom.

~~49~~56. The method of any one of claims 1-~~48~~55, wherein the sample comprises one or more host cell proteins, and wherein one of the one or more host cell proteins is a hydrolytic enzyme.

~~50~~57. The method of claim ~~49~~56, wherein the hydrolytic enzyme is a lipase, an esterase, a thioesterase, a phospholipase, or a ceramidase.

~~51~~58. The method of any one of claims 1-~~50~~57, wherein the sample comprises a target, and wherein the target is an antibody moiety.

~~52~~59. The method of claim ~~51~~58, wherein the antibody moiety is a monoclonal antibody.

~~53~~60. The method of claim ~~51~~ 58 or ~~52~~59, wherein the antibody moiety is a human, humanized, or chimeric antibody.

~~54~~61. The method of any one of claims ~~51~~58-~~53~~60, wherein the antibody moiety is selected from the group consisting of an anti-CD20 antibody, an anti-CD40 antibody, an anti-HER2 antibody, an anti-IL6 antibody, an anti-IgE antibody, an anti-IL13 antibody, an anti-TIGIT antibody, an anti-PD-L1 antibody, an anti-VEGF-A antibody, an anti-VEGF-A/ANG2 antibody, an anti-CD79b antibody, an anti-ST2 antibody, an anti-factor D antibody, an anti-factor IX antibody, an anti-factor X antibody, an anti-abeta antibody, an anti-tau antibody, an

anti-CEA antibody, an anti-CEA/CD3 antibody, an anti-CD20/CD3 antibody, an anti-FcRH5/CD3 antibody, an anti-Her2/CD3 antibody, an anti-FGFR1/KLB antibody, a FAP-4-1 BBL fusion protein, a FAP-IL2v fusion protein, and a TYRP1 TCB antibody.

~~55~~62. The method of any one of claims ~~51~~58-~~54~~61, wherein the antibody moiety is selected from the group consisting of ocrelizumab, pertuzumab, trastuzumab, tocilizumab, faricimab, polatuzumab, gantenerumab, cibisatamab, crenezumab, mosunetuzumab, tiragolumab, bevacizumab, rituximab, atezolizumab, obinutuzumab, lampalizumab, lebrikizumab, omalizumab ranibizumab, emicizumab, selicrelumab, prasinezumab, RO6874281, and RO7122290.

~~56. A pharmaceutical composition obtained from the method of any one of claims 1-55.~~

~~57~~63. The method of any one of claims 1-62~~A formulated antibody moiety composition comprising an antibody moiety and a polysorbate wherein the composition has a reduced polysorbate hydrolysis activity rate~~, wherein the shelf-life of the composition is more than 24 months.

~~58~~64. The method of any one of claims 1-63~~A formulated antibody moiety composition comprising an antibody moiety and a polysorbate, wherein the composition has a reduced polysorbate hydrolysis activity rate, wherein the shelf-life of the composition is extended compared to the shelf-life indicated in documents filed with a health authority related to the formulated antibody moiety composition~~, wherein the shelf-life of the composition is extended by at least 6 months compared to a shelf-life of a composition obtained from purification of the sample using the same purification platform without the depth filter comprising cellulose fibers, diatomaceous earth, and perlite~~the shelf-life indicated in said documents~~.

~~59. A formulated antibody moiety composition comprising an antibody moiety, wherein the formulated antibody moiety composition has a reduced degradation of polysorbate, wherein the degradation is reduced by at least about 20% compared to the degradation indicated in documents filed with a health authority related to the formulated antibody moiety composition.~~

60. A formulated antibody moiety composition comprising an antibody moiety and a polysorbate, wherein the polysorbate is degraded during storage of the liquid composition by 20% or less per year.

61. The formulated antibody moiety composition of any one of claims 57-60, wherein the antibody moiety is a monoclonal antibody.

62. The formulated antibody moiety composition of any one of claims 57-61, wherein the antibody moiety is a human, humanized, or chimeric antibody.

63. The formulated antibody moiety composition of any one of claims 57-62, wherein the antibody is selected from the group consisting of an anti-CD20 antibody, an anti-CD40 antibody, an anti-HER2 antibody, an anti-IL6 antibody, an anti-IgE antibody, an anti-IL13 antibody, an anti-TIGIT antibody, an anti-PD-L1 antibody, an anti-VEGF-A antibody, an anti-VEGF-A/ANG2 antibody, an anti-CD79b antibody, an anti-ST2 antibody, an anti-factor D antibody, an anti-factor IX antibody, an anti-factor X antibody, an anti-abeta antibody, an anti-tau antibody, an anti-CEA antibody, an anti-CEA/CD3 antibody, an anti-CD20/CD3 antibody, an anti-FcRH5/CD3 antibody, an anti-Her2/CD3 antibody, an anti-FGFR1/KLB antibody, a FAP-4-1 BBL fusion protein, a FAP-IL2v fusion protein, and a TYRP1 TCB antibody.

64. The formulated antibody moiety composition of any one of claims 57-63, wherein the antibody moiety is selected from the group consisting of ocrelizumab, pertuzumab, trastuzumab, tocilizumab, faricimab, polatuzumab, gantenerumab, cibisatamab, crenezumab, mosunetuzumab, tiragolumab, bevacizumab, rituximab, atezolizumab, obinutuzumab, lampalizumab, lebrikizumab, omalizumab ranibizumab, emicizumab, selicrelumab, prasinezumab, RO6874281, and RO7122290.

65. The formulated antibody moiety composition of any one of claims 57-64, wherein the polysorbate hydrolysis activity rate is reduced by at least about 20%.

66. The formulated antibody moiety composition of any one of claims 57-65, wherein the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80.

67. A method of reducing an enzymatic hydrolysis activity rate of a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in order:

(a) a capture step comprising processing via affinity chromatography; and

(b) a purification step comprising processing via a chromatography selected from the group consisting of a HIC, a cation exchange chromatography, and a multimodal chromatography,

wherein the purification platform further comprises one or more depth filtration steps,

wherein the one or more depth filtration steps are performed at any one or more of: prior to the capture step; after the capture step; or after the capture step and prior to the purification step,

wherein each depth filtration step comprises processing via a depth filter, and

wherein the depth filter comprises materials selected from the group consisting of:

(i) a silica and a polyacrylic fiber;

(ii) a hydrogel Q (quaternary amine) functionalized non-woven media and a multi-zone microporous membrane; and

(iii) cellulose fibers, diatomaceous earth, and perlite,

thereby reducing the enzymatic hydrolysis activity rate of the composition as compared to purification of the sample using the same purification platform without the one or more depth filtration steps.

68. The method of claim 67, wherein the enzymatic hydrolysis activity rate is an enzymatic polysorbate hydrolysis activity rate.

69. The method of claim 67 or 68, wherein the relative reduction of the enzymatic hydrolysis activity rate of the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 20%.

70. A method of reducing the level of one or more hydrolytic enzymes in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in order:

(a) a capture step comprising processing via affinity chromatography; and

(b) a purification step comprising processing via a chromatography selected from the group consisting of a HIC, a cation exchange chromatography, and a multimodal chromatography,

wherein the purification platform further comprises one or more depth filtration steps,

wherein the one or more depth filtration steps are performed at any one or more of: prior to the capture step; after the capture step and prior to the purification step; or after the purification step,

wherein each depth filtration step comprises processing via a depth filter, and

wherein the depth filter comprises materials selected from the group consisting of:

(i) a silica and a polyacrylic fiber;

(ii) a hydrogel Q (quaternary amine) functionalized non-woven media and a multi-zone microporous membrane; and

(iii) cellulose fibers, diatomaceous earth, and perlite,

thereby reducing the level of one or more hydrolytic enzymes in the composition as compared to purification of the sample using the same purification platform without the one or more depth filtration steps.

71. The method of claim 70, wherein the one or more hydrolytic enzymes are capable of hydrolyzing a polysorbate.

72. The method of claim 70 or 71, wherein the relative reduction of the level of one or more hydrolytic enzymes in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 20%.

73. A method of reducing degradation of a polysorbate in a composition obtained from a purification platform, the method comprising subjecting a sample to the purification platform comprising, in order:

(a) a capture step comprising processing via affinity chromatography; and

(b) a purification step comprising processing via a chromatography selected from the group consisting of a HIC, a cation exchange chromatography, and a multimodal chromatography,

wherein the purification platform further comprises one or more depth filtration steps,

wherein the one or more depth filtration steps are performed at any one or more of: prior to the capture step; after the capture step; or after the capture step and prior to the purification step,

wherein each depth filtration step comprises processing via a depth filter, and

wherein the depth filter comprises materials selected from the group consisting of:

(i) a silica and a polyacrylic fiber;

(ii) a hydrogel Q (quaternary amine) functionalized non-woven media and a multi-zone microporous membrane; and

(iii) cellulose fibers, diatomaceous earth, and perlite,

thereby reducing degradation of a polysorbate in the composition as compared to purification of the sample using the same purification platform without the one or more depth filtration steps.

74. The method of claim 73, wherein the relative reduction of degradation of the polysorbate in the composition, as compared to purification of the sample using the same purification platform without the depth filtration step, is at least about 5%.

75. The method of any one of claims 67-74, wherein the depth filter comprising the silica and the polyacrylic fiber comprises a silica filter aid and a polyacrylic fiber pulp.

76. The method of any one of claims 67-74, wherein the depth filter comprising the hydrogel Q-functionalized non-woven media and the multi-zone microporous membrane comprises four layers comprising hydrogel Q-functionalized non-woven materials and a nine-zone microporous membrane.

77. The method of any one of claims 67-74, wherein the depth filter comprising cellulose fibers, diatomaceous earth, and perlite comprises two layers, wherein each layer comprises a

cellulose filter matrix, wherein the cellulose filter matrix is impregnated with a filter aid comprising one or more of diatomaceous earth or perlite, and wherein each layer further comprises a resin binder.

78. The method of any one of claims 67-77, wherein the depth filter is selected based on the pH of the solution entering the depth filter.

79. The method of claim 78, wherein the depth filter comprising the silica and the polyacrylic fiber is selected when the solution entering the depth filter is about 5 to about 6.5.

80. The method of claim 78, wherein the depth filter comprising the hydrogel Q-functionalized non-woven media and the multi-zone microporous membrane is selected when the solution entering the depth filter is about 7 to about 8.5.

81. The method of any one of claims 67-80, further comprising selecting the depth filter based on the pH of the solution entering the depth filter.

82. The method of any one of claims 67-81, wherein the purification platform comprises, in order, a depth filtration step comprising processing via the depth filter comprising the hydrogel Q-functionalized non-woven media and a multi-zone microporous membrane, the capture step comprising processing via a protein A chromatography, and the purification step.

83. The method of claim 82, wherein the purification step comprises processing via the HIC.

84. The method of claim 83, wherein the HIC is a phenyl SEPHAROSE® fast flow chromatography.

85. The method of claim 82, wherein the purification step comprises processing via the cation exchange chromatography.

86. The method of claim 85, wherein the cation exchange chromatography is POROS® 50HS.

87. The method of any one of claims 67-86, wherein the purification platform further comprises a second depth filtration step comprising processing via the depth filter comprising the silica

and the polyacrylic fiber, and wherein the second depth filtration step occurs after the capture step and prior to the purification step.

88. The method of claim 82, wherein the purification step comprises processing via the multimodal chromatography.

89. The method of claim 88, wherein the multimodal chromatography is Capto Adhere.

90. The method of claim 88 or 89, wherein the purification platform further comprises a second depth filtration step comprising processing via the depth filter comprising the hydrogel Q-functionalized non-woven media and a multi-zone microporous membrane, and wherein the second depth filtration step occurs after the capture step and prior to the purification step.

91. The method of any one of claims 67-90, wherein the purification platform is for purification of a target from the sample, wherein the sample comprises the target and one or more host cell impurities.

92. The method of claim 91, wherein the target comprises a polypeptide.

93. The method of claim 91 or 92, wherein the host cell impurity is a host cell protein.

94. The method of any one of claims 67-93, wherein the purification platform further comprises a virus inactivation step, wherein the virus inactivation step is performed after the capture step.

95. The method of claim 94, wherein the one or more depth filtration steps are performed after the virus inactivation step.

96. The method of any one of claims 67-95, wherein the purification platform further comprises an ultrafiltration/diafiltration (UFDF) step, and wherein the UFDF step is performed after the purification step.

97. The method of any one of claims 67-96, further comprising determining the enzymatic hydrolysis activity rate of the composition.

98. The method of any one of claims 67-97, further comprising determining the level of one or more hydrolytic enzymes in the composition.

99. The method of any one of claims 67-98, wherein the composition comprises a polysorbate.

100. The method of claim 99, wherein the polysorbate is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 60, and polysorbate 80.

101. The method of any one of claims 67-100, further comprising a sample processing step.

102. The method of any one of claims 67-101, wherein the sample is, or is derived from, a cell culture sample.

103. The method of claim 102, wherein the cell culture sample comprises a host cell, and wherein the host cell is a Chinese hamster ovary (CHO) cell or an *E. coli* cell.

104. The method of any one of claims 67-103, wherein the sample comprises a host cell or components originating therefrom.

105. The method of any one of claims 67-104, wherein the sample comprises one or more host cell proteins, and wherein one of the one or more host cell proteins is a hydrolytic enzyme.

106. The method of claim 105, wherein the hydrolytic enzyme is a lipase, an esterase, a thioesterase, a phospholipase, or a ceramidase.

107. The method of any one of claims 67-106, wherein the sample comprises a target, and wherein the target is an antibody moiety.

108. The method of claim 107, wherein the antibody moiety is a monoclonal antibody.

109. The method of claim 107 or 108, wherein the antibody moiety is a human, humanized, or chimeric antibody.

110. The method of any one of claims 107-109, wherein the antibody moiety is selected from the group consisting of an anti-CD20 antibody, an anti-CD40 antibody, an anti-HER2 antibody,

~~an anti-IL6 antibody, an anti-IgE antibody, an anti-IL13 antibody, an anti-TIGIT antibody, an anti-PD-L1 antibody, an anti-VEGF-A antibody, an anti-VEGF-A/ANG2 antibody, an anti-CD79b antibody, an anti-ST2 antibody, an anti-factor D antibody, an anti-factor IX antibody, an anti-factor X antibody, an anti-abeta antibody, an anti-tau antibody, an anti-CEA antibody, an anti-CEA/CD3 antibody, an anti-CD20/CD3 antibody, an anti-FcRH5/CD3 antibody, an anti-Her2/CD3 antibody, an anti-FGFR1/KLB antibody, a FAP-4-1 BBL fusion protein, a FAP-IL2v fusion protein, and a TYRP1 TCB antibody.~~

~~111. The method of any one of claims 107-110, wherein the antibody moiety is selected from the group consisting of ocrelizumab, pertuzumab, trastuzumab, tocilizumab, faricimab, polatuzumab, gantenerumab, cibisatamab, crenezumab, mosunetuzumab, tiragolumab, bevacizumab, rituximab, atezolizumab, obinutuzumab, lampalizumab, lebrikizumab, omalizumab ranibizumab, emicizumab, selicrelumab, prasinezumab, RO6874281, and RO7122290.~~

~~112. A pharmaceutical composition obtained from the method of any one of claims 67-111.~~