BRIEF SUMMARY

[10] Disclosed herein are methods of treating an IL-17-dependent condition, comprising administering a medicament comprising an IL-17A- and/or IL-17F-inhibiting nanobody to a subject wherein the subject has been identified as having an elevated level of one or more biomarkers selected from IL6, PLA2G2A, IL19, PI3, CST7, IL17A, IL17F, GH1, MZB1, IL1B, IFNG, TNC, CXCL9, SLAMF7, VEGFA, IL17C, SLAMF1, SDC1, OSM, LBP, REG3A, CD79B, COL4A1, CLEC4D, VWF, IL5RA, CSF3, TGFA, IL2RA, ITIH3, FCAR, CCL23, NRCAM, RETN, SERPINA11, CLEC4G, CSF1, HGF, CRELD2, EFEMP1, LTBR, NME3, CKAP4, CD276, SPON2, GGH, TIMP1, LY9, MCFD2, TCN2, QPCT, HYOU1, TNSFSF13B, CCL2, CCL3, CCL4, CCL5, CCL7, CCL20, CXCL1, CXCL8, PDFGA, CXCR2, CCR6, and CXCL13.

[11] Also disclosed herein are methods of treating hidradenitis suppurativa (HS), comprising administering a medicament comprising an IL-17A- and/or IL-17F-inhibitor to a subject, wherein the subject has been identified as having an elevated level of one or more biomarkers selected from IL6, PLA2G2A, IL19, PI3, CST7, IL17A, IL17F, GH1, MZB1, IL1B, IFNG, TNC, CXCL9, SLAMF7, VEGFA, IL17C, SLAMF1, SDC1, OSM, LBP, REG3A, CD79B, COL4A1, CLEC4D, VWF, IL5RA, CSF3, TGFA, IL2RA, ITIH3, FCAR, CCL23, NRCAM, RETN, SERPINA11, CLEC4G, CSF1, HGF, CRELD2, EFEMP1, LTBR, NME3, CKAP4, CD276, SPON2, GGH, TIMP1, LY9, MCFD2, TCN2, QPCT, HYOU1, TNSFSF13B, CCL2, CCL3, CCL4, CCL5, CCL7, CCL20, CXCL1, CXCL8, PDFGA, CXCR2, CCR6, and CXCL13. In examples, such a method is contemplated, wherein the IL-17A- and/or IL-17F-inhibitor comprises a nanobody.

[12] Methods of treatment as above are also disclosed, wherein the nanobody is configured to specifically bind to IL-17A and IL-17F, preferably the nanobody is sonelokimab (SLK).

[13] Methods of treatment as above are also disclosed, wherein the elevated level is as compared to: (i) the level present in non-lesional skin, preferably in perilesional skin, (ii) the level present in peripheral blood of a healthy patient, or (iii) the level in the same subject prior to initial treatment.

[14] Methods of treatment as above are also disclosed, wherein the elevated level is as compared to a reference value and the reference value is (i) the biomarker's expression level from the corresponding body fluid or tissue sample obtained from a healthy subject; (ii) the average level of the biomarker expressed in the corresponding body fluid or tissue of a plurality of healthy subjects; or (iii) the average level of the biomarker expressed in healthy tissue, preferably healthy tissue from the same subject, more preferably perilesional skin from the same subject.

NRCAM, RETN, SERPINA11, CLEC4G, CSF1, HGF, CRELD2, EFEMP1, LTBR, NME3, CKAP4, CD276, SPON2, GGH, TIMP1, LY9, MCFD2, TCN2, QPCT, HYOU1, TNSFSF13B, CCL2, CCL3, CCL4, CCL5, CCL7, PDFGA, CXCR2, CCR6, and CXCL13.

[24] Methods of treatment as above are also disclosed, wherein the one or more biomarkers are selected from CSF3, CCL2, CCL3, CCL4, CCL5, CCL7, CCL20, CXCL1, CXCL8, and PDFGA.

[25] Methods of treatment as above are also disclosed, wherein the one or more biomarkers are selected from CCL20, CXCL8, CXCL1, IL17A, and IL17F.

[26] Also disclosed herein is use of an agent that selectively binds to IL-17A and/or IL-17F in a subject determined to have an elevated level of at least one of the following biomarkers: IL6, PLA2G2A, IL19, PI3, CST7, IL17A, IL17F, GH1, MZB1, IL1B, IFNG, TNC, CXCL9, SLAMF7, VEGFA, IL17C, SLAMF1, SDC1, OSM, LBP, REG3A, CD79B, COL4A1, CLEC4D, VWF, IL5RA, CSF3, TGFA, IL2RA, ITIH3, FCAR, CCL23, NRCAM, RETN, SERPINA11, CLEC4G, CSF1, HGF, CRELD2, EFEMP1, LTBR, NME3, CKAP4, CD276, SPON2, GGH, TIMP1, LY9, MCFD2, TCN2, QPCT, HYOU1, TNSFSF13B, CCL2, CCL3, CCL4, CCL5, CCL7, CCL20, CXCL1, CXCL8, PDFGA, CXCR2, CCR6, and CXCL13 compared to a healthy control, preferably wherein the elevated level is present in the skin and/or in the blood, for the use according to the present disclosure and any example, any combination, and/or any group of biomarkers disclosed apply accordingly.

[27] A use as above is also disclosed, wherein the elevated level of the at least one biomarker is the level present in a biological sample from the subject, and the level of the corresponding at least biomarker present in the healthy control is representative of the level present in a biological sample not affected by an IL-17-dependent condition, preferably by an IL-17-dependent inflammatory skin disease, more preferably by hidradenitis suppurativa (HS).

[28] A use as above is also disclosed, wherein the biomarkers are associated with an inflammatory skin disease, preferably an inflammatory skin disease afflicting both the epidermis and dermis, more preferably an inflammatory skin disease involving hair follicle structures, even more preferably an inflammatory skin disease involving acneiform lesions, most preferably hidradenitis suppurativa (HS).

[29] A use as above is also disclosed, which is characterized by an elevated mRNA level or elevated protein level of at least one or more biomarkers selected from IL6, PLA2G2A, IL19, PI3, CST7, IL17A, IL17F, GH1, MZB1, IL1B, IFNG, TNC, CXCL9, SLAMF7,

VEGFA, IL17C, SLAMF1, SDC1, OSM, LBP, REG3A, CD79B, COL4A1, CLEC4D, VWF, IL5RA, CSF3, TGFA, IL2RA, ITIH3, FCAR, CCL23, NRCAM, RETN, SERPINA11, CLEC4G, CSF1, HGF, CRELD2, EFEMP1, LTBR, NME3, CKAP4, CD276, SPON2, GGH, TIMP1, LY9, MCFD2, TCN2, QPCT, HYOU1, TNSFSF13B, CCL2, CCL3, CCL4, CCL5, CCL7, CCL20, CXCL1, CXCL8, PDFGA, CXCR2, CCR6, and CXCL13, and preferably from at least one or more biomarkers selected from CCL20, CXCL8, CXCL1, IL17A, and IL17F.

[30] A use as above is also disclosed, which is characterized by an elevated mRNA level or elevated protein level in a lesional skin sample compared to the respective mRNA or protein level of a non-lesional skin sample.

[31] A use as above is also disclosed, wherein a lesional IL-17F / non-lesional IL-17 mRNA ratio or protein ratio is determined.

[32] A use as above is also disclosed, wherein the subject has been identified as having an inflammatory skin disease, preferably an inflammatory skin disease afflicting both the epidermis and dermis, more preferably an inflammatory skin disease involving hair follicle structures, even more preferably an inflammatory skin disease involving acneiform lesions, most preferably hidradenitis suppurativa, respectively exhibiting an elevated level of one or more biomarkers.

[33] A use as above is also disclosed, wherein the subject has been clinically diagnosed as having HS in Hurley Stage I or II or III.

[34] A use as above is also disclosed, wherein the release of IL-17A and/or IL-17F in Hurley Stage I, II and/or III of hidradenitis suppurativa is inhibited by the agent.

[35] A use as above is also disclosed, wherein the agent is an IL-17A- and/or IL-17F-inhibitor.

[36] A use as above is also disclosed, wherein inflammation and/or tissue destruction is inhibited.

[37] A use as above is also disclosed, wherein the agent comprises an antibody, an antibody fragment, or a nanobody. In examples of such a use, the agent may comprise a nanobody, preferably the nanobody is sonelokimab or a derivative thereof.

[38] A use as above is also disclosed, wherein the agent is a nanobody, preferably sonelokimab or a derivative thereof, and a biomarker panel comprises a) CCL20, CXCL1, CXCL8, CXL1, IL17A, IL17F, IL19, LT01, CSF3, OSM, PLA2G2A, CST7 and/or PI3, b) IL17A, IL17F, CCL20, CXCL1, and/or CXCL8, c) IL17A, IL17F, CCL20, and/or CXCL8, d) LT01, IL17A, CSF3, OSM, PLA2G2A and/or CST7, e) CCL20, CXCL8, IL19, and PI3; or f) PI3 and IL19.

an agent configured to inhibit IL-17F present in the dermis of an inflammatory skin lesion of the subject.

[61] Also disclosed herein is a method of treating a subject having an assayed lesional IL-17F / non-lesional IL-17F mRNA ratio 5 or higher, preferably 10 or higher, more preferably 5-500, and most preferably 10-300, which comprises administering an effective amount of an agent configured to inhibit IL-17F present in the dermis of an inflammatory skin lesion of the subject.

[62] Also disclosed herein is a method of treating hidradenitis suppurativa, comprising administering a medicament comprising an IL-17A- and/or IL-17F-inhibitor to a subject, wherein the subject has been identified as having elevated levels of one or more biomarkers selected from (a) LTO1, (b) CSF3, (c) OSM, (d) PLA2G2A, or (e) a combination of IL17A and TNC.

[63] Also disclosed herein, in an aspect, is a method of identifying a patient having hidradenitis suppurativa, which patient is responsive to treatment with an IL-17A- and/or IL-17F-inhibiting nanobody, comprising assaying a biological sample from the patient for the presence of one or more biomarkers selected from (a) LTO1, (b) CSF3, (c) OSM, (d) PLA2G2A, or (e) a combination of IL17A and TNC, wherein the presence of an elevated level of at least one, two, three, or more of the biomarkers indicates that the patient is responsive to treatment with an IL-17A- and/or IL-17F-inhibiting nanobody.

[64] Such a method of identifying may comprise identifying a patient who is a super-responder.

[65] Also disclosed herein is such a method of identifying, wherein the identified patient is administered treatment with an IL-17A- and/or IL-17F-inhibiting nanobody, preferably sonelokimab.

[66] Also disclosed herein is such a method of identifying, wherein the nanobody comprises sonelokimab.

[67] Also disclosed herein is a kit for identifying a subject at risk or in need of treatment for an IL-17-dependent condition, which kit comprises a reagent or reagents for measuring the level or expression of one or more of: IL6, PLA2G2A, IL19, PI3, CST7, IL17A, IL17F, GH1, MZB1, IL1B, IFNG, TNC, CXCL9, SLAMF7, VEGFA, IL17C, SLAMF1, SDC1, OSM, LBP, REG3A, CD79B, COL4A1, CLEC4D, VWF, IL5RA, CSF3, TGFA, IL2RA, ITIH3, FCAR, CCL23, NRCAM, RETN, SERPINA11, CLEC4G, CSF1, HGF, CRELD2, EFEMP1, LTBR, NME3, CKAP4, CD276, SPON2, GGH, TIMP1, LY9, MCFD2, TCN2, QPCT, HYOU1, TNSFSF13B, CCL2, CCL3, CCL4, CCL5, CCL7, CCL20, CXCL1, CXCL8, PDFGA, CXCR2, CCR6, CXCL13, PCDH1, BOC, MEPE, ADAM23, THOP1, IL1RL2, RCOR1, and EDAR.

CLAIMS

1. A method of identifying a patient having hidradenitis suppurativa, which patient is responsive to treatment with an IL-17A- and/or IL-17F-inhibiting nanobody, comprising assaying a biological sample from the patient for the presence of one or more biomarkers selected from (a) LTO1, (b) CSF3, (c) OSM, (d) PLA2G2A, or (e) a combination of IL17A and TNC, wherein the presence of an elevated level of at least one, two, three, or more of the biomarkers indicates that the patient is responsive to treatment with an IL-17A- and/or IL-17F-inhibiting nanobody.

2. The method of claim 1, which comprises identifying a patient who is a super-responder.

3. The method of claim 1 or 2, wherein the identified patient is to be administered treatment with an IL-17A- and/or IL-17F-inhibiting nanobody, preferably sonelokimab.

4. The method of any of claims 1-3, wherein the nanobody comprises sonelokimab.