

CLAIMS:

1. A humanized monoclonal IgG antibody wherein the variable domains are represented by a combination of V_{HH} -derivative with a variable domain of the light chain V_L .
2. An antibody according to Claim 1, characterized by increased aggregation stability of V_{HH} -derivative compared to the native VHH antibody isolated from an immunized animal from Camelidae family.
3. An antibody according to Claim 1, wherein the V_{HH} -derivative comprises the following amino acid substitutions at positions 44X₂45X₃:
 - a) wherein 44X₂ = G, A, V, S, T;
 - b) wherein 45X₃ = A, V, T, H;or combinations thereof.
4. An antibody according to Claim 3, characterized by increased aggregation stability of V_{HH} -derivative compared to the native VHH antibody isolated from an immunized animal from Camelidae family.
5. An antibody according to Claim 1, wherein the V_{HH} -derivative is represented by a variable domain of the heavy chain isolated from an immunized animal from Camelidae family and comprises additional amino acid substitutions typical for humans and located at any positions, except for the following substitutions at positions 44X₂45X₃:
 - c) wherein 44X₂ = G, A, V, S, T;
 - d) wherein 45X₃ = A, V, T, H;or combinations thereof.
6. An antibody according to Claim 1, wherein V_{HH} -derivative is a

variable domain of the heavy chain isolated from a non-immunized animal from Camelidae family, and comprises additional amino acid substitutions typical for humans and located at any positions, except for the following substitutions at positions 44X₂45X₃:

- e) wherein 44X₂ = G, A, V, S, T;
 - f) wherein 45X₃ = A, V, T, H;
- or combinations thereof.

7. An antibody according to Claim 1, wherein the variable domain of the light chain V_L is a human antibody derivative.

8. An antibody according to Claim 1, wherein the variable domain of the light chain V_L is a humanized fragment of an antibody, preferably mammalian.

9. An antibody according to Claim 1, wherein V_{HH}-derivative that contains cysteine-44 (Kabat numbering scheme), and a light chain variable domain V_L contains cysteine-100 (Kabat numbering scheme).

10. An antibody according to Claim 1, wherein said antibody is one of any of the following isotypes: IgG1, IgG2, IgG3 or IgG4.

11. An antibody according to Claim 10, comprising a non-native modified Fc as a part of IgG.

12. An antibody according to Claim 1, characterized by such aggregation stability that when used in concentrations over 10 mg/ml and stored for >6 months at a temperature of 4⁰C the content of aggregates increases by not more than 5% of their initial content in the solution.

13. An antibody according to Claim 1, characterized by such aggregation stability that when used in concentrations over 10 mg/ml and stored for >2 weeks at a temperature of 37⁰C the content of aggregates increases by not more than 5% of their initial content in the solution.

14. An antibody according to Claim 1, characterized by such aggregation stability that when used in concentrations over 10 mg/ml and stored for >48h at a temperature of 42⁰C the content of aggregates increases by not more than 5% of their initial content in the solution.

15. An antibody according to Claim 1, characterized by such aggregation stability that when used in concentrations over 10 mg/ml and stored for > 6 h at a temperature of 50⁰C the content of aggregates increases by not more than 5% of their initial content in the solution.

16. An antibody according to Claim 1, wherein the dissociation constant K_D is 10⁻⁹ M and lower.

17. An antibody according to Claim 1, wherein the antibody-antigen interaction kinetic association constant k_{on} (1/Ms) is at least 10⁵ 1/Msec and more.

18. An antibody according to Claim 1, wherein the antibody-antigen interaction kinetic dissociation constant $dis(1/c)$ is 10⁻⁴ 1/sec and lower.

19. An antibody according to Claims 1-18 that specifically binds to human IL-17A, comprising

a) a derivative of Camelidae heavy chain variable domain (V_{HH}) that comprises 3 hypervariable regions HCDR1, HCDR2 and HCDR3, whereinde:

HCDR1 comprising the amino acid sequence of SEQ ID NO: 1:

G-T-F-A-T-X32-X33-X34 - X35, где

X32 is an amino acid selected from the group comprising S, N, K, R, E, W, Q, D, A, V and F;

X33 is an amino acid selected from the group comprising P or S;

X34 is an amino acid selected from the group comprising M and I;

X35 is an amino acid selected from the group comprising G, N, S, A, L, I, R, V and Q;

HCDR2 comprising the amino acid sequence of SEQ ID NO: 2:

X50-I-X52-X52a-S-G-X55-D-R-I-Y-A-D-S-V-K-G, где

X50 is an amino acid selected from the group comprising A, G and L;

X52 is an amino acid selected from the group comprising S, D and E;

X52a is an amino acid selected from the group comprising P and A;

X55 is an amino acid selected from the group comprising G,S,T, L, R, D, E, K, A and W;

HCDR3 comprising the amino acid sequence of SEQ ID NO: 3:

C-A- X94-X95- X96- X97-F-X99-X100-X100a- X100b - X100c - X100d - X100e - X100f – D- Y – D-S, где

X94 is an amino acid selected from the group comprising K, S, T, V, D and G;

X95 is an amino acid selected from the group comprising R and K;

X96 is an amino acid selected from the group comprising G, R, Y, H, D, W and K;

X97 is an amino acid selected from the group comprising R, A, V, S, L and H;

X99 is an amino acid selected from the group comprising D, E, G, A, R, V, K and Q;

X100 is an amino acid selected from the group comprising G, S and N;

X100a is an amino acid selected from the group comprising G, T, P, V, R, N and K;

X100b is an amino acid selected from the group comprising V, S, T, L, Y, A, H, G and I;

X100c is an amino acid selected from the group comprising Y, W and S;

X100d is an amino acid selected from the group comprising R, V, L, Y, A, W, K, G, Q and I;

X100e is an amino acid selected from the group comprising T, L, A and S;

X100f is an amino acid selected from the group comprising T, L, G, P, N, A, Q, F, I and D;

b) a variable domain of the light chain (V_L) of a human antibody or a variable domain of the light chain of a humanized antibody.

20. An antibody according to Claims 1-18 that specifically binds to human IL-17A, comprising:

a) A derivative of the heavy chain variable domain (V_{HH}) comprising 3 hypervariable regions HCDR1, HCDR2 и HCDR3, wherein:

HCDR1 comprising the amino acid sequence of G-T-F-A-T-S-P-M-G (SEQ ID NO: 4);

HCDR2 comprising the amino acid sequence of A-I-S-P-S-G-G- D-R-I-Y-A-D-S-V-K-G (SEQ ID NO: 5);

HCDR3 comprising the amino acid sequence of C-A-V-R-R-R-F-D-G-T-S-Y-Y-T-G-D-Y-D-S (SEQ ID NO: 6);

b) A variable domain of the light chain (V_L) of a human antibody or a variable domain of the light chain of a humanized antibody.

21. An antibody according to Claim 20 that specifically binds to human IL-17A, comprising:

a) A derivative of the heavy chain variable domain (V_{HH}) comprising an amino acid sequence

QVQLVQSGGGLVQAGGSLRLSCAASGGTFATSPMGWLRQAPGKGT
EFVAAISPSGGDRIYADSVKGRFTISRDNAGYFIYLMNSLKPEDTAVYYC
AVRRRFDGTSYYTGDYDSWGQGTLLTVSS (SEQ ID NO: 7);

b) A variable domain of the light chain (V_L) of a human antibody or a variable domain of the light chain of a humanized antibody.

22. An antibody according to Claim 21 that specifically binds to human IL-17A, comprising V_{HH} -derivative, wherein said variable domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 7.

23. An antibody according to Claim 22 that specifically binds to human IL-17A, comprising:

a) The V_{HH} -derivative comprising the amino acid sequence of SEQ ID NO: 7;

b) The variable domain of the light chain (V_L) of a human antibody comprising the amino acid sequence of

EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWEYQQKPGQAPRLL
IYDASSRATGIPDRFSGSGGTDFTLISRLEPEDFAVYYCQQYSYSPVTFGQ
GTKVEIKR (SEQ ID NO: 8).

24. An antibody according to Claim 23 that specifically binds human IL-17A and comprises V_{HH} -derivative and a variable region of the light chain (V_L) of a human antibody, wherein said variable domains comprise an amino acid sequence at least 90% identical to SEQ ID NO: 8.

25. An antibody according to Claims 1-18 that specifically binds human IL-17A and comprises:

a) The heavy chain comprising the following amino acid sequence:

QVQLVQSGGGLVQAGGSLRLSCAASGGTFATSPMGWLRQAPGKGT
EFVAAISPSGGDRIYADSVKGRFTISRDNAGYFIYLMNSLKPEDTAVYYC

AVRRRFDGTSYYTGDYDSWGQGLVTVSSASTKGPSVFPLAPSSKSTSGGT
AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS
SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVF
LFPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKP
REEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY
KTTTPVLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSL
SLSPGK (SEQ ID NO: 9).

b) The variable domain of a human antibody light chain (V_L) comprising the following amino acid sequence:

EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRL
IYDASSRATGIPDRFSGSGGTDFTLTISRLEPEDFAVYYCQQYSYSPVTFGQ
GTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVD
NALQSGNSQESVTEQDSKSTYLSSTLTLSKADYEEKHKVYACEVTHQGL
SSPVTKSFNRGEC (SEQ ID NO: 10).

26. An antibody according to Claim 25 that specifically binds human IL-17A and contains the heavy chain and the light chain, wherein said chains comprise amino acid sequences at least 90% identical to SEQ ID NO: 9 and/or SEQ ID NO:10.

27. An antibody according to Claim 19, wherein said antibody has the binding affinity to human IL-17A characterized with K_D of 10^{-10} M and lower.

28. An antibody according to Claim 19, wherein the kinetic association constant $k_{on}(1/Mc)$ for human IL-17A is not less than 10^5 1/Msec.

29. An antibody according to Claim 19, wherein the kinetic dissociation constant $k_{\text{dis}}(1/\text{s})$ for human IL-17A is not more than $10^{-5} 1/\text{sec}$.

30. An antibody according to Claim 19, wherein said antibody inhibits the activity of human IL-17A by no less than.

31. An antibody according to Claim 19, wherein said antibody is produced by mammalian, yeast or bacterial cells.

32. An antibody according to Claim 19 comprising one or more additional amino acid substitutions in Fc-region compared to the native Fc, wherein said substitutions improve physical-chemical and pharmacokinetic properties of an antibody, as compared to an antibody with the native Fc, and do not result in the loss of antibody's ability to bind IL-17A.

33. Fragment of an antibody according to Claims 1- 32.

34. Fragment of an antibody according to Claim 33, wherein said fragment is represented by a light chain, heavy chain, and variable domains of the light and/or heavy chain that are a part of an antibody sequence, which includes a bio-specific antibody variant.

35. Fragment of an antibody according to Claim 34, wherein said fragment is represented by a light chain, heavy chain, and variable domains of the light and/or heavy chain that are parts of Fab.

36. Fragment of an antibody according to Claim 34, wherein said fragment is represented by a light chain, heavy chain, and variable domains of the light and/or heavy chain that are parts of scFv.

37. Methods of production of antibodies according to any of Claims 1 – 32 or fragments thereof according to Claims 33-36, involving phases selected from the following: directed mutagenesis, display methods, genetic engineering, biochemistry and high-performance biotechnology methods well known for the art, which can include the methods for directed mutagenesis at different positions of the VHH domain of Camelidae antibodies.

38. A DNA construct encoding an antibody according to any of Claims 1 - 32 or an antibody fragment according to any of Claims 33-36.

39. An expression vector comprising one or several DNA constructs according to Claim 38.

40. A cell line comprising the expression vector according to Claim 39 or DNA construct according to Claim 38.

41. Method of production of a humanized monoclonal antibody according to Claims 1- 32 or an antibody fragment according to Claims 33-36, which involves incubation of a cell line according to Claim 40 in a culture medium under the conditions sufficient to obtain said antibody or fragment thereof, followed by the isolation and purification of obtained antibody or its active fragment.

42. A host cell comprising the vector according to Claim 39.

43. Method of production of an antibody according to any of Claims 1-32 or an antibody fragment according to Claims 33-36, which involves incubation of a cell line according to Claim 42 in a culture medium under the conditions sufficient

to obtain said antibody or fragment thereof, followed by isolation and purification of obtained antibody or its active fragment

44. A pharmaceutical composition comprising an antibody according to any of Claims 1-32 or fragments thereof according to Claims 33-36, in combination with one or several pharmaceutically suitable excipients, diluents or carriers.

45. A pharmaceutical composition according to Claim 44, further comprising active pharmaceutical ingredients selected from TNF- α inhibitors.

46. A pharmaceutical composition according to Claim 44, to be used in the therapy of IL-17A-mediated disease or disorder.

47. A pharmaceutical composition according to Claim 46, wherein an IL-17A-mediated disease or disorder is selected from: rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, septic arthritis, Lyme arthritis, psoriatic arthritis, reactive arthritis, spondyloarthropathy, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, inflammatory bowel disease, insulin dependent diabetes mellitus, thyroidenitis, asthma, allergic disorders, psoriasis, dermatitis, systemic sclerosis, graft-versus-host disease, graft rejection, acute or chronic immune disease associated with organ grafting, sarcoidosis, atherosclerosis, disseminated intravascular coagulation, Kawasaki disease, Graves' disease, nephrotic syndrome, chronic fatigue syndrome, Wegener's disease, Henoch-Schonlein purpura, microscopic polyangiitis with renal involvement, chronic active hepatitis, uveitis, septic shock, toxic shock syndrome, sepsis syndrome, cachexia, infections, invasions, acquired immune deficiency syndrome, acute transverse myelitis, Huntington chorea, Parkinson disease, Alzheimer disease, stroke, primary biliary cirrhosis, hemolytic anemia, malignancies, heart failure, myocardial infarction, Addison disease, polyglandular autoimmune syndrome type I and type II, Schmidt's syndrome, acute respiratory distress syndrome, alopecia, alopecia

areata, seronegative arthropathy, arthropathy, Reiter's syndrome, psoriatic arthropathy, arthropathy associated with ulcerative colitis, enteropathic synovitis, arthropathy associated with Chlamydia, Yersinia and Salmonella, spondyloarthropathy, atheromatosis disease/coronary sclerosis, atopic allergy, autoimmune bullous disease, pemphigus, pemphigus foliaceus, pemphigoid, linear iga diseases, autoimmune hemolytic anemia, Coombs positive hemolytic anemia, acquired pernicious anemia, juvenile pernicious anemia, Myalgic encephalomyelitis/chronic fatigue syndrome, chronic active hepatic inflammation, cranial giant arteritis, primary sclerosing hepatitis, cryptogenic autoimmune hepatitis, acquired immune deficiency syndrome (AIDS), AIDS-associated diseases, hepatitis B, hepatitis C, common variable immunodeficiency (common variable hypogammaglobulinemia), dilated cardiomyopathy, female sterility, ovarian insufficiency, Premature ovarian failure, pulmonary fibrosis, cryptogenic fibrosing alveolitis, post inflammatory interstitial lung pathologies, interstitial pneumonitis, connective tissue disease associated with interstitial lung disease, mixed connective tissue disease associated with interstitial lung disease, systemic scleroderma associated with interstitial lung disease, rheumatoid arthritis associated with interstitial lung disease, systemic lupus erythematosus associated with lung disease, dermatomyositis/polymyositis associated with lung disease, Sjogren disease associated with lung disease, ankylosing spondylitis associated with lung disease, diffuse pulmonary vasculitis, hemosiderosis associated with lung disease, drug-induced interstitial lung disease, fibrosis, radiation-induced fibrosis, obliterating bronchiolitis, chronic eosinophilic pneumonia, lung disease with lymphocyte infiltration, post infectious interstitial lung pathologies, gouty arthritis, autoimmune hepatitis, autoimmune hepatitis type I (classic autoimmune or lupoid hepatitis), autoimmune hepatitis type II (associated with anti-LKM antibody), autoimmune hypoglycemia, type B insulin resistance with acanthokeratoderma, hypoparathyroidism, acute graft-associated immune disease, chronic graft-associated immune disease, osteoarthritis, primary sclerosing cholangitis, type I psoriasis, type II psoriasis, idiopathic leukopenia, autoimmune

neutropenia, NOS-kidney diseases, glomerulonephritis, microscopic renal polyangiitis, Lyme disease, discoid lupus erythematosus, idiopathic of NOS-male sterility, antisperm immunity, multiple sclerosis (all types), sympathetic ophthalmia, pulmonary hypertension secondary to connective tissue disease, Goodpasture syndrome, pulmonary manifestations of polyarteritis nodosa, acute rheumatic fever, rheumatoid spondylitis, Still's disease, systemic scleroderma, Sjogren's Syndrome, Takayasu disease/arthritis, autoimmune thrombocytopenia, idiopathic thrombocytopenia, autoimmune thyroid disorders, hyperthyroid, autoimmune hypothyroidism (Hashimoto disease), atrophic autoimmune hypothyroidism, primary myxedema, phacogenic uveitis, primary vasculitis, vitiligo, acute hepatic disease, chronic hepatic disease, alcoholic cirrhosis, alcohol-induced liver damage, cholestasis, idiosyncratic hepatic disease, drug-induced hepatitis, nonalcoholic steatohepatitis, allergies and asthma, group B streptococcal infection (GBS), mental disorders (including depressions and schizophrenia), Th1- and Th2-mediated disease, acute and chronic pain (various forms), malignancies such as lung cancer, breast cancer, stomach cancer, bladder cancer, colorectal cancer, pancreatic cancer, ovarian cancer, prostate cancer and hematopoietic malignancies (leukemia and lymphomas), abetalipoproteinaemia, acrocyanosis, acute and chronic infections and infestations, acute leukemia, acute lymphoblastic leukemia, acute myeloid leukemia, acute or chronic bacterial infection, acute pancreatitis, acute renal failure, adenocarcinoma, atrial ectopics, AIDS dementia complex, alcohol-induced hepatitis, allergic conjunctivitis, allergic contact dermatitis, allergic rhinitis, allograft rejection, alpha-I antitrypsin deficiency, lateral amyotrophic sclerosis, anemia, angina, anterior horn cell degeneration, anti-CD3 therapy, antiphospholipid syndrome, hypersensitivity reactions against receptors, aortic and peripheral aneurysms, aortic dissection, arterial hypertension, coronary sclerosis, arteriovenous fistula, ataxia, atrial fibrillation (constant or paroxysmal), atrial flutter, atrioventricular block, B-cell lymphoma, bone graft rejection, bone marrow transplant (BMT) rejection, bundle branch block, Burkitt lymphoma, burns, cardiac arrhythmia, myocardial stunning syndrome, cardiac

tumor, cardiomyopathy, inflammatory response to bypass, cartilage graft rejection, brain cortex degeneration, cerebellar disorder, chaotic or multifocal atrial tachycardia, chemotherapy-induced disorders, chronic myelocytic leukemia (CML), chronic alcohol addiction, chronic inflammatory pathologies, chronic lymphatic leukemia (CLL), chronic obstructive pulmonary disease, chronic salicylate intoxication, rectocolic carcinoma, congestive cardiac failure, conjunctivitis, contact dermatitis, pulmonary heart, coronary artery disease, Creutzfeldt-Jakob Disease, culture-negative sepsis, cystic fibrosis, cytokine therapy-induced disorders, boxer's encephalopathy, demyelinating disease, dengue hemorrhagic fever, dermatitis, dermatological conditions, diabetes, diabetes mellitus, diabetes-related atherosclerotic vascular disease, diffuse Lewy body disease, congestive dilated cardiomyopathy, basal ganglia disease, Down's syndrome in middle age, motor disorders induced by CNS dopamine blockers, drug sensitivity, eczema, encephalomyelitis, endocarditis, endocrinopathy, epiglottiditis, Epstein-Barr viral infection, erythralgia, extrapyramidal and cerebellar symptoms, familial hemophagocytic lymphohistiocytosis, fetal thymus graft rejection, Friedreich's ataxia, peripheral artery disease, fungal sepsis, gas phlegmon, gastric ulcer, glomerulonephritis, any organ or tissue graft rejection, gram negative sepsis, gram positive sepsis, granulomas due to intracellular organisms, hairy-cell leukemia, Hallervorden-Spatz disease, Hashimoto's thyroiditis, hay fever, heart transplant rejection, hemochromatosis, hemodialysis, hemolytic uremic syndrome / thrombotic thrombocytopenic purpura, bleeding, hepatitis (A), bundle branch arrhythmia, HIV-infections/HIV-neuropathies, Hodgkin disease, hyperkinetic motor disorders, hypersensitivity reactions, hypersensitivity-associated pneumonitis, hypertension, hypokinetic motor disorders, examination of hypothalamo-pituitary-adrenal axis, idiopathic Addison's disease, idiopathic pulmonary fibrosis, antibody-mediated cytotoxicity, asthenia, infantile muscular atrophy, aortal inflammation, influenza virus A, exposure to ionizing radiation, iridocyclitis /uveitis/optic neuritis, ischaemia/reperfusion-induced disorders, ischaemic stroke, juvenile rheumatoid arthritis, juvenile spinal

muscular atrophy, Kaposi's sarcoma, renal transplant rejection, legionellosis, leishmaniasis, leprosy, corticospinal damage, lipodema, liver transplant rejection, lymphoedema, malaria, malignant lymphoma, malignant histiocytosis, malignant melanoma, meningitis, meningococemia, metabolic/idiopathic diseases, migraine, multiple system mitochondrial disorders, mixed connective-tissue disease, monoclonal gammopathy, multiple myeloma, multiple system degeneration (Mencel Dejerine-Thomas Shi-Drager and Machado-Joseph), myasthenia gravis, intracellular Mycobacterium avium, Mycobacterium tuberculosis, myelodysplastic syndrome, myocardial infarction, myocardial ischemic disease, nasopharyngeal cancer, neonatal chronic lung disease, nephritis, nephrotic, neurodegenerative disorders, neurogenic muscular atrophy I, neutropenic fever, non-Hodgkin's lymphomas, abdominal aortic branch occlusion, arterial occlusive disease, OKT3® treatment, orchitis/epididymitis, orchitis/vasectomy reversal operations, organomegaly, osteoporosis, pancreatic graft rejection, pancreatic carcinoma, paraneoplastic disease /tumor-related hypercalcemia, parathyroid graft rejection, pelvic inflammatory disease, perennial rhinitis, pericardial disease, peripheral atherosclerosis (atherosclerotic) disease, peripheral vascular disease, peritonitis, pernicious anemia, Pneumocystis carinii pneumonia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma-proliferative disorder and skin changes), postperfusion syndrome, pump head syndrome, post-cardiotomy post-infarction syndrome, preeclampsia, progressive supranuclear paralysis, primary pulmonary hypertension, radiation therapy, Raynaud's phenomenon and disease, Raynaud's disease, Refsum's disease, regular narrow QRS tachycardia, renal vascular hypertension, reperfusion injury, restrictive cardiomyopathy, sarcoma, scleroderma disease, senile chorea, Dementia with Lewy bodies, seronegative arthritis, shock, sickle cell disease, skin allograft rejection, skin changes, small intestinal graft rejection, solid tumors, specific arrhythmias, spinal ataxia, spinocerebellar degradations, streptococcal myositis, cerebellar structural damage, subacute sclerosing panencephalitis, syncope, cardiovascular syphilis, systemic anaphylaxis, a comprehensive systemic

inflammatory response syndrome, systemic-onset juvenile rheumatoid arthritis, T cells or FAB ALL, telangiectasia, thrombosis obliterans, thrombocytopenia, toxicity, grafting, trauma/bleeding, hypersensitivity reactions type III, hypersensitivity reactions type IV, unstable angina, uremia, urinary sepsis, urticaria, valvular heart disease, varicose veins, vasculitis, venous diseases, venous thrombosis, ventricular fibrillation, viral and fungal infections, viral encephalitis / aseptic meningitis, viral hemophagocytic syndrome, Wernicke-Korsakoff syndrome, Wilson's disease, heterograft rejection for any organ or tissue, acute coronary syndrome, acute idiopathic polyneuritis, acute inflammatory demyelinating radicular neuropathy, acute ischemia, adult-onset Stills disease, alopecia areata, anaphylaxis, antiphospholipid antibody syndrome, aplastic anemia, coronary sclerosis, atopic eczema, atopic dermatitis, autoimmune dermatitis, autoimmune disorder associated with streptococcus infection, autoimmune enteropathy, autoimmune hearing loss, autoimmune lymphoproliferative syndrome (ALPS), autoimmune myocarditis, autoimmune premature ovarian failure, blepharitis, bronchiectasis, bullous pemphigoid, cardiovascular disease, catastrophic antiphospholipid syndrome, celiac disease, cervical spondylosis, chronic ischemia, cicatricial pemphigoid, clinically isolated syndrome (cis) with the risk for multiple sclerosis, conjunctivitis, childhood-onset mental disorders, chronic obstructive pulmonary disease (COPD), dacryocystitis, dermatomyositis, diabetic retinopathy, diabetes mellitus, herniated disk, prolapse of intervertebral disc, drug-induced immune haemolytic anaemia, endocarditis, endometreosis, entophthalmia, episcleritis, erythema multiform, severe erythema multiform, gestational pemphigoid , Guillain-Barre syndrome (GBS), hay fever, Hughes syndrome, idiopathic Parkinson's disease, idiopathic interstitial pneumonia, IgE-mediated allergy, autoimmune hemolytic anemia, inclusion body myositis, infectious ocular inflammatory disease, inflammatory demyelinating disease, inflammatory heart disease, inflammatory kidney disease, idiopathic pulmonary fibrosis/ usual interstitial pneumonia, iritis, кератита, keratitis, keratoconjunctivitis sicca, Kussmaul disease or Kussmaul-Meier Disease, Landry palsy, Langerhans'

cell histiocytosis, marbled skin, macular degeneration, microscopic polyangiitis, Bechterew disease, motor neuron disease, mucosal pemphigoid, multiple organ failure, myasthenia gravis, spinal cord dysplasia syndrome, myocarditis, nerve root disorders, neuropathy, non-A, non-B hepatitis, optic neuritis, osteolysis, ovarian cancer, oligoarticular JIA, peripheral arterial occlusive disease, peripheral vascular disease, peripheral artery disease (PAD), phlebitis, polyarteritis nodosa, polychondritis, polymyalgia rheumatica, poliosis, polyarticular juvenile idiopathic arthritis, multiple endocrine deficiency, polymyositis, polymyalgia rheumatica (PMR), post pump syndrome, primary parkinsonism, prostate and rectal cancer and hematopoietic malignancies (leukemia and lymphoma), prostatitis, pure red-cell aplasia, primary adrenal insufficiency, relapsing neuromyelitis optica, restenosis, rheumatic heart disease, SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis), scleroderma, secondary amyloidosis, shock lung, scleritis, ischias, secondary adrenal insufficiency, silicon-associated connective tissue disease, Sneddon-Wilkinson disease, ankylosing spondylitis, Stevens–Johnson syndrome, systemic inflammation response syndrome, cranial arteritis, Toxoplasma rhinitis, toxic epidermal necrolysis, transverse myelitis, TRAPS (tumor necrosis factor receptor-associated periodic syndrome), allergic reactions type I, diabetes type II, urticaria, usual interstitial pneumonia, vasculitis, vernal conjunctivitis, viral retinitis, Vogt-Koyanagi-Harada syndrome (VKH syndrome), wet macular degeneration, wound healing, and Yersinia- or Salmonella-associated arthropathy.

48. The use of the isolated antibody according to Claims 1-32 or fragment thereof according to Claims 33-36 in the treatment of IL-17A-mediated disease or disorder, characterized by its administration of a therapeutically effective amount to a patient who needs such a treatment.

49. The use according to Claim 48, wherein an IL-17A-mediated disease or disorder is selected from: rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, septic arthritis, Lyme arthritis, psoriatic arthritis, reactive arthritis,

spondyloarthropathy, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, inflammatory bowel disease, insulin dependent diabetes mellitus, thyroadenitis, asthma, allergic disorders, psoriasis, dermatitis, systemic sclerosis, graft-versus-host disease, graft rejection, acute or chronic immune disease associated with organ grafting, sarcoidosis, atherosclerosis, disseminated intravascular coagulation, Kawasaki disease, Graves' disease, nephrotic syndrome, chronic fatigue syndrome, Wegener's disease, Henoch-Schonlein purpura, microscopic polyangiitis with renal involvement, chronic active hepatitis, uveitis, septic shock, toxic shock syndrome, sepsis syndrome, cachexia, infections, invasions, acquired immune deficiency syndrome, acute transverse myelitis, Huntington chorea, Parkinson disease, Alzheimer disease, stroke, primary biliary cirrhosis, hemolytic anemia, malignancies, heart failure, myocardial infarction, Addison disease, polyglandular autoimmune syndrome type I and type II, Schmidt's syndrome, acute respiratory distress syndrome, alopecia, alopecia areata, seronegative arthropathy, arthropathy, Reiter's syndrome, psoriatic arthropathy, arthropathy associated with ulcerative colitis, enteropathic synovitis, arthropathy associated with Chlamydia, Yersinia and Salmonella, spondyloarthropathy, atheromatosis disease/coronary sclerosis, atopic allergy, autoimmune bullous disease, pemphigus, pemphigus foliaceus, pemphigoid, linear iga diseases, autoimmune hemolytic anemia, Coombs positive hemolytic anemia, acquired pernicious anemia, juvenile pernicious anemia, Myalgic encephalomyelitis/chronic fatigue syndrome, chronic active hepatic inflammation, cranial giant arteritis, primary sclerosing hepatitis, cryptogenic autoimmune hepatitis, acquired immune deficiency syndrome (AIDS), AIDS-associated diseases, hepatitis B, hepatitis C, common variable immunodeficiency (common variable hypogammaglobulinemia), dilated cardiomyopathy, female sterility, ovarian insufficiency, Premature ovarian failure, pulmonary fibrosis, cryptogenic fibrosing alveolitis, post inflammatory interstitial lung pathologies, interstitial pneumonitis, connective tissue disease associated with interstitial lung disease, mixed connective tissue disease associated with interstitial lung disease, systemic scleroderma associated with interstitial lung

disease, rheumatoid arthritis associated with interstitial lung disease, systemic lupus erythematosus associated with lung disease, dermatomyositis/polymyositis associated with lung disease, Sjogren disease associated with lung disease, ankylosing spondylitis associated with lung disease, diffuse pulmonary vasculitis, hemosiderosis associated with lung disease, drug-induced interstitial lung disease, fibrosis, radiation-induced fibrosis, obliterating bronchiolitis, chronic eosinophilic pneumonia, lung disease with lymphocyte infiltration, post infectious interstitial lung pathologies, gouty arthritis, autoimmune hepatitis, autoimmune hepatitis type I (classic autoimmune or lupoid hepatitis), autoimmune hepatitis type II (associated with anti-LKM antibody), autoimmune hypoglycemia, type B insulin resistance with acanthokeratoderma, hypoparathyroidism, acute graft-associated immune disease, chronic graft-associated immune disease, osteoarthritis, primary sclerosing cholangitis, type I psoriasis, type II psoriasis, idiopathic leukopenia, autoimmune neutropenia, NOS-kidney diseases, glomerulonephritis, microscopic renal polyangiitis, Lyme disease, discoid lupus erythematosus, idiopathic of NOS-male sterility, antisperm immunity, multiple sclerosis (all types), sympathetic ophthalmia, pulmonary hypertension secondary to connective tissue disease, Goodpasture syndrome, pulmonary manifestations of polyarteritis nodosa, acute rheumatic fever, rheumatoid spondylitis, Still's disease, systemic scleroderma, Sjogren's Syndrome, Takayasu disease/arthritis, autoimmune thrombocytopenia, idiopathic thrombocytopenia, autoimmune thyroid disorders, hyperthyroid, autoimmune hypothyroidism (Hashimoto disease), atrophic autoimmune hypothyroidism, primary myxedema, phacogenic uveitis, primary vasculitis, vitiligo, acute hepatic disease, chronic hepatic disease, alcoholic cirrhosis, alcohol-induced liver damage, cholestasis, idiosyncratic hepatic disease, drug-induced hepatitis, nonalcoholic steatohepatitis, allergies and asthma, group B streptococcal infection (GBS), mental disorders (including depressions and schizophrenia), Th1- and Th2-mediated disease, acute and chronic pain (various forms), malignancies such as lung cancer, breast cancer, stomach cancer, bladder cancer, colorectal cancer, pancreatic cancer, ovarian cancer, prostate cancer and hematopoietic

malignancies (leukemia and lymphomas), abetalipoproteinaemia, acrocyanosis, acute and chronic infections and infestations, acute leukemia, acute lymphoblastic leukemia, acute myeloid leukemia, acute or chronic bacterial infection, acute pancreatitis, acute renal failure, adenocarcinoma, atrial ectopics, AIDS dementia complex, alcohol-induced hepatitis, allergic conjunctivitis, allergic contact dermatitis, allergic rhinitis, allograft rejection, alpha-I antitrypsin deficiency, lateral amyotrophic sclerosis, anemia, angina, anterior horn cell degeneration, anti-CD3 therapy, antiphospholipid syndrome, hypersensitivity reactions against receptors, aortic and peripheral aneurysms, aortic dissection, arterial hypertension, coronary sclerosis, arteriovenous fistula, ataxia, atrial fibrillation (constant or paroxysmal), atrial flutter, atrioventricular block, B-cell lymphoma, bone graft rejection, bone marrow transplant (BMT) rejection, bundle branch block, Burkitt lymphoma, burns, cardiac arrhythmia, myocardial stunning syndrome, cardiac tumor, cardiomyopathy, inflammatory response to bypass, cartilage graft rejection, brain cortex degeneration, cerebellar disorder, chaotic or multifocal atrial tachycardia, chemotherapy-induced disorders, chronic myelocytic leukemia (CML), chronic alcohol addiction, chronic inflammatory pathologies, chronic lymphatic leukemia (CLL), chronic obstructive pulmonary disease, chronic salicylate intoxication, rectocolic carcinoma, congestive cardiac failure, conjunctivitis, contact dermatitis, pulmonary heart, coronary artery disease, Creutzfeldt-Jakob Disease, culture-negative sepsis, cystic fibrosis, cytokine therapy-induced disorders, boxer's encephalopathy, demyelinating disease, dengue hemorrhagic fever, dermatitis, dermatological conditions, diabetes, diabetes mellitus, diabetes-related atherosclerotic vascular disease, diffuse Lewy body disease, congestive dilated cardiomyopathy, basal ganglia disease, Down's syndrome in middle age, motor disorders induced by CNS dopamine blockers, drug sensitivity, eczema, encephalomyelitis, endocarditis, endocrinopathy, epiglottiditis, Epstein-Barr viral infection, erythralgia, extrapyramidal and cerebellar symptoms, familial hemophagocytic lymphohistiocytosis, fetal thymus graft rejection, Friedreich's ataxia, peripheral artery disease, fungal sepsis, gas

phlegmon, gastric ulcer, glomerulonephritis, any organ or tissue graft rejection, gram negative sepsis, gram positive sepsis, granulomas due to intracellular organisms, hairy-cell leukemia, Hallervorden-Spatz disease, Hashimoto's thyroiditis, hay fever, heart transplant rejection, hemochromatosis, hemodialysis, hemolytic uremic syndrome / thrombotic thrombocytopenic purpura, bleeding, hepatitis (A), bundle branch arrhythmia, HIV-infections/HIV-neuropathies, Hodgkin disease, hyperkinetic motor disorders, hypersensitivity reactions, hypersensitivity-associated pneumonitis, hypertension, hypokinetic motor disorders, examination of hypothalamo-pituitary-adrenal axis, idiopathic Addison's disease, idiopathic pulmonary fibrosis, antibody-mediated cytotoxicity, asthenia, infantile muscular atrophy, aortal inflammation, influenza virus A, exposure to ionizing radiation, iridocyclitis /uveitis/optic neuritis, ischaemia/reperfusion-induced disorders, ischaemic stroke, juvenile rheumatoid arthritis, juvenile spinal muscular atrophy, Kaposi's sarcoma, renal transplant rejection, legionellosis, leishmaniasis, leprosy, corticospinal damage, lipodema, liver transplant rejection, lymphoedema, malaria, malignant lymphoma, malignant histiocytosis, malignant melanoma, meningitis, meningococemia, metabolic/idiopathic diseases, migraine, multiple system mitochondrial disorders, mixed connective-tissue disease, monoclonal gammopathy, multiple myeloma, multiple system degeneration (Mencel Dejerine-Thomas Shi-Drager and Machado-Joseph), myasthenia gravis, intracellular Mycobacterium avium, Mycobacterium tuberculosis, myelodysplastic syndrome, myocardial infarction, myocardial ischemic disease, nasopharyngeal cancer, neonatal chronic lung disease, nephritis, nephrotic, neurodegenerative disorders, neurogenic muscular atrophy I, neutropenic fever, non-Hodgkin's lymphomas, abdominal aortic branch occlusion, arterial occlusive disease, OKT3® treatment, orchitis/epididymitis, orchitis/vasectomy reversal operations, organomegaly, osteoporosis, pancreatic graft rejection, pancreatic carcinoma, paraneoplastic disease /tumor-related hypercalcemia, parathyroid graft rejection, pelvic inflammatory disease, perennial rhinitis, pericardial disease, peripheral atherosclerosis (atherlosclerotic) disease, peripheral vascular disease, peritonitis,

pernicious anemia, Pneumocystis carinii pneumonia, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma-proliferative disorder and skin changes), postperfusion syndrome, pump head syndrome, post-cardiotomy post-infarction syndrome, preeclampsia, progressive supranuclear paralysis, primary pulmonary hypertension, radiation therapy, Raynaud's phenomenon and disease, Raynaud's disease, Refsum's disease, regular narrow QRS tachycardia, renal vascular hypertension, reperfusion injury, restrictive cardiomyopathy, sarcoma, scleroderma disease, senile chorea, Dementia with Lewy bodies, seronegative arthritis, shock, sickle cell disease, skin allograft rejection, skin changes, small intestinal graft rejection, solid tumors, specific arrhythmias, spinal ataxia, spinocerebellar degenerations, streptococcal myositis, cerebellar structural damage, subacute sclerosing panencephalitis, syncope, cardiovascular syphilis, systemic anaphylaxis, a comprehensive systemic inflammatory response syndrome, systemic-onset juvenile rheumatoid arthritis, T cells or FAB ALL, telangiectasia, thrombosis obliterans, thrombocytopenia, toxicity, grafting, trauma/bleeding, hypersensitivity reactions type III, hypersensitivity reactions type IV, unstable angina, uremia, urinary sepsis, urticaria, valvular heart disease, varicose veins, vasculitis, venous diseases, venous thrombosis, ventricular fibrillation, viral and fungal infections, viral encephalitis / aseptic meningitis, viral hemophagocytic syndrome, Wernicke-Korsakoff syndrome, Wilson's disease, heterograft rejection for any organ or tissue, acute coronary syndrome, acute idiopathic polyneuritis, acute inflammatory demyelinating radicular neuropathy, acute ischemia, adult-onset Still's disease, alopecia areata, anaphylaxis, antiphospholipid antibody syndrome, aplastic anemia, coronary sclerosis, atopic eczema, atopic dermatitis, autoimmune dermatitis, autoimmune disorder associated with streptococcus infection, autoimmune enteropathy, autoimmune hearing loss, autoimmune lymphoproliferative syndrome (ALPS), autoimmune myocarditis, autoimmune premature ovarian failure, blepharitis, bronchiectasis, bullous pemphigoid, cardiovascular disease, catastrophic antiphospholipid syndrome, celiac disease, cervical spondylosis,

chronic ischemia, cicatrical pemphigoid, clinically isolated syndrome (cis) with the risk for multiple sclerosis, conjunctivitis, childhood-onset mental disorders, chronic obstructive pulmonary disease (COPD), dacryocystitis, dermatomyositis, diabetic retinopathy, diabetes mellitus, herniated disk, prolapse of intervertebral disc, drug-induced immune haemolytic anaemia, endocarditis, endometreosis, entophthalmia, episcleritis, erythema multiform, severe erythema multiform, gestational pemphigoid , Guillain-Barre syndrome (GBS), hay fever, Hughes syndrome, idiopathic Parkinson's disease, idiopathic interstitial pneumonia, IgE-mediated allergy, autoimmune hemolytic anemia, inclusion body myositis, infectious ocular inflammatory disease, inflammatory demyelinating disease, inflammatory heart disease, inflammatory kidney disease, idiopathic pulmonary fibrosis/ usual interstitial pneumonia, iritis, гепатита, keratitis, keratoconjunctivitis sicca, Kussmaul disease or Kussmaul-Meier Disease, Landry palsy, Langerhans' cell histiocytosis, marbled skin, macular degeneration, microscopic polyangiitis, Bechterew disease, motor neuron disease, mucosal pemphigoid, multiple organ failure, myasthenia gravis, spinal cord dysplasia syndrome, myocarditis, nerve root disorders, neuropathy, non-A, non-B hepatitis, optic neuritis, osteolysis, ovarian cancer, oligoarticular JIA, peripheral arterial occlusive disease, peripheral vascular disease, peripheral artery disease (PAD), phlebitis, polyarteritis nodosa, polychondritis, polymyalgia rheumatica, poliosis, polyarticular juvenile idiopathic arthritis, multiple endocrine deficiency, polymyositis, polymyalgia rheumatica (PMR), post pump syndrome, primary parkinsonism, prostate and rectal cancer and hematopoietic malignancies (leukemia and lymphoma), prostatitis, pure red-cell aplasia, primary adrenal insufficiency, relapsing neuromyelitis optica, restenosis, rheumatic heart disease, SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis), scleroderma, secondary amyloidosis, shock lung, scleritis, ischias, secondary adrenal insufficiency, silicon-associated connective tissue disease, Sneddon-Wilkinson disease, ankylosing spondylitis, Stevens–Johnson syndrome, systemic inflammation response syndrome, cranial arteritis, Toxoplasma rhinitis, toxic epidermal necrolysis, transverse myelitis, TRAPS (tumor necrosis factor

receptor-associated periodic syndrome), allergic reactions type I, diabetes type II, urticaria, usual interstitial pneumonia, vasculitis, vernal conjunctivitis, viral retinitis, Vogt-Koyanagi-Harada syndrome (VKH syndrome), wet macular degeneration, wound healing, and Yersinia- or Salmonella-associated arthropathy.

50. The use according to 49, further comprising the administration of TNF- α inhibitors.