(2) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 55; SEQ ID NO: 59; SEQ ID NO: 60 and SEQ ID NO: 61; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:64, SEQ ID NO:68 and SEQ ID NO: 69;

(3) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 84; SEQ ID NO: 88; SEQ ID NO: 89; SEQ ID NO: 90; SEQ ID NO: 121; SEQ ID NO: 122; and SEQ ID NO: 123; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:91, SEQ ID NO:95 and SEQ ID NO:96;

(4) the variable heavy chain amino acid sequence set forth in SEQ ID NO:112 and the variable light chain amino acid sequence set forth in SEQ ID NO:103;

(5) the variable heavy chain amino acid sequence set forth in SEQ ID NO:113 and the variable light chain amino acid sequence set forth in SEQ ID NO:104;

(6) the variable heavy chain amino acid sequence set forth in SEQ ID NO:114 and the variable light chain amino acid sequence set forth in SEQ ID NO:105;

(7) the variable heavy chain amino acid sequence set forth in SEQ ID NO:116 and the variable light chain amino acid sequence set forth in SEQ ID NO:107;

(8) the variable heavy chain amino acid sequence set forth in SEQ ID NO:117 and the variable light chain amino acid sequence set forth in SEQ ID NO:108;

(9) the variable heavy chain amino acid sequence set forth in SEQ ID NO:118 and the variable light chain amino acid sequence set forth in SEQ ID NO:109;

(10) the variable heavy chain amino acid sequence set forth in SEQ ID NO:119 and the variable light chain amino acid sequence set forth in SEQ ID NO:110; and

(11) the variable heavy chain amino acid sequence set forth in SEQ ID NO:120 and the variable light chain amino acid sequence set forth in SEQ ID NO:111.

In another aspect, the invention pertains binding protein capable of binding PRLR that competes with an antibody comprising a heavy chain variable domain and a light chain variable domain selected from the group consisting of:

(1) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 39; SEQ ID NO: 43; SEQ ID NO: 44 and SEQ ID NO: 45; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO: 53 and SEQ ID NO:54;

(2) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 55; SEQ ID NO: 59; SEQ ID NO: 60 and SEQ ID NO: 61; and a

variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:64, SEQ ID NO:68 and SEQ ID NO: 69;

(3) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 84; SEQ ID NO: 88; SEQ ID NO: 89; SEQ ID NO: 90; SEQ ID NO: 121; SEQ ID NO: 122; and SEQ ID NO: 123; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:91, SEQ ID NO:95 and SEQ ID NO:96;

(4) the variable heavy chain amino acid sequence set forth in SEQ ID NO:112 and the variable light chain amino acid sequence set forth in SEQ ID NO:103;

(5) the variable heavy chain amino acid sequence set forth in SEQ ID NO:113 and the variable light chain amino acid sequence set forth in SEQ ID NO:104;

(6) the variable heavy chain amino acid sequence set forth in SEQ ID NO:114 and the variable light chain amino acid sequence set forth in SEQ ID NO:105;

(7) the variable heavy chain amino acid sequence set forth in SEQ ID NO:116 and the variable light chain amino acid sequence set forth in SEQ ID NO:107;

(8) the variable heavy chain amino acid sequence set forth in SEQ ID NO:117 and the variable light chain amino acid sequence set forth in SEQ ID NO:108;

(9) the variable heavy chain amino acid sequence set forth in SEQ ID NO:118 and the variable light chain amino acid sequence set forth in SEQ ID NO:109;

(10) the variable heavy chain amino acid sequence set forth in SEQ ID NO:119 and the variable light chain amino acid sequence set forth in SEQ ID NO:110; and

(11) the variable heavy chain amino acid sequence set forth in SEQ ID NO:120 and the variable light chain amino acid sequence set forth in SEQ ID NO:111;

wherein the binding protein is a monoclonal antibody.

In another embodiment, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, competes with an antibody comprising a heavy chain variable domain and a light chain variable domain selected from the group consisting of:

(1) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 39; SEQ ID NO: 43; SEQ ID NO: 44 and SEQ ID NO: 45; and a variable light chain having an amino acid sequence selected from the group consisting of SEQ ID NO:48, SEQ ID NO:52, SEQ ID NO: 53 and SEQ ID NO:54;

(2) a variable heavy chain having an amino acid sequence selected from the group consisting of SEQ ID NO: 55; SEQ ID NO: 59; SEQ ID NO: 60 and SEQ ID NO: 61; and a

In another aspect, the invention pertains to a binding protein capable of binding PRLR that competes with an antibody comprising a heavy chain sequence and a light chain sequence selected from the group consisting of:

(a) a heavy chain having the amino acid sequence of SEQ ID NO: 124; and a light chain having the amino acid sequence of SEQ ID NO: 125;

(b) a heavy chain having the amino acid sequence of SEQ ID NO: 124; and a light chain having the amino acid sequence of SEQ ID NO: 126;

(c) a heavy chain having the amino acid sequence of SEQ ID NO: 124; and a light chain having the amino acid sequence of SEQ ID NO: 127;

(d) a heavy chain having the amino acid sequence of SEQ ID NO: 124; and a light chain having the amino acid sequence of SEQ ID NO: 128;

(e) a heavy chain having the amino acid sequence of SEQ ID NO: 129; and a light chain having the amino acid sequence of SEQ ID NO: 125;

(f) a heavy chain having the amino acid sequence of SEQ ID NO: 129; and a light chain having the amino acid sequence of SEQ ID NO: 126;

(g) a heavy chain having the amino acid sequence of SEQ ID NO: 129; and a light chain having the amino acid sequence of SEQ ID NO: 127;

(h) a heavy chain having the amino acid sequence of SEQ ID NO: 129; and a light chain having the amino acid sequence of SEQ ID NO: 128;

(i) a heavy chain having the amino acid sequence of SEQ ID NO: 130; and a light chain having the amino acid sequence of SEQ ID NO: 125;

(j) a heavy chain having the amino acid sequence of SEQ ID NO: 130; and a light chain having the amino acid sequence of SEQ ID NO: 126;

(k) a heavy chain having the amino acid sequence of SEQ ID NO: 130; and a light chain having the amino acid sequence of SEQ ID NO: 127;

(l) a heavy chain having the amino acid sequence of SEQ ID NO: 130; and a light chain having the amino acid sequence of SEQ ID NO: 128;

(m) a heavy chain having the amino acid sequence of SEQ ID NO: 131; and a light chain having the amino acid sequence of SEQ ID NO: 132;

(n) a heavy chain having the amino acid sequence of SEQ ID NO: 131; and a light chain having the amino acid sequence of SEQ ID NO: 133;

(o) a heavy chain having the amino acid sequence of SEQ ID NO: 131; and a light chain having the amino acid sequence of SEQ ID NO: 134;

(p) a heavy chain having the amino acid sequence of SEQ ID NO: 135; and a light chain having the amino acid sequence of SEQ ID NO: 132;

(q) a heavy chain having the amino acid sequence of SEQ ID NO: 135; and a light chain having the amino acid sequence of SEQ ID NO: 133;

(r) a heavy chain having the amino acid sequence of SEQ ID NO: 135; and a light chain having the amino acid sequence of SEQ ID NO: 134;

(s) a heavy chain having the amino acid sequence of SEQ ID NO: 136; and a light chain having the amino acid sequence of SEQ ID NO: 132;

(t) a heavy chain having the amino acid sequence of SEQ ID NO: 136; and a light chain having the amino acid sequence of SEQ ID NO: 133;

(u) a heavy chain having the amino acid sequence of SEQ ID NO: 136; and a light chain having the amino acid sequence of SEQ ID NO: 134;

(v) a heavy chain having the amino acid sequence of SEQ ID NO: 137; and a light chain having the amino acid sequence of SEQ ID NO: 138;

(w) a heavy chain having the amino acid sequence of SEQ ID NO: 137; and a light chain having the amino acid sequence of SEQ ID NO: 139;

(x) a heavy chain having the amino acid sequence of SEQ ID NO: 137; and a light chain having the amino acid sequence of SEQ ID NO: 140;

(y) a heavy chain having the amino acid sequence of SEQ ID NO: 141; and a light chain having the amino acid sequence of SEQ ID NO: 138;

(z) a heavy chain having the amino acid sequence of SEQ ID NO: 141; and a light chain having the amino acid sequence of SEQ ID NO: 139;

(aa) a heavy chain having the amino acid sequence of SEQ ID NO: 141; and a light chain having the amino acid sequence of SEQ ID NO: 140;

(bb) a heavy chain having the amino acid sequence of SEQ ID NO: 142; and a light chain having the amino acid sequence of SEQ ID NO: 138;

(cc) a heavy chain having the amino acid sequence of SEQ ID NO: 142; and a light chain having the amino acid sequence of SEQ ID NO: 139;

(dd) a heavy chain having the amino acid sequence of SEQ ID NO: 142; and a light chain having the amino acid sequence of SEQ ID NO: 140;

(ee) a heavy chain having the amino acid sequence of SEQ ID NO: 143; and a light chain having the amino acid sequence of SEQ ID NO: 144;

(ff) a heavy chain having the amino acid sequence of SEQ ID NO: 143; and a light chain having the amino acid sequence of SEQ ID NO: 145;

(gg) a heavy chain having the amino acid sequence of SEQ ID NO: 143; and a light chain having the amino acid sequence of SEQ ID NO: 146;

(hh) a heavy chain having the amino acid sequence of SEQ ID NO: 147; and a light chain having the amino acid sequence of SEQ ID NO: 144;

(ii) a heavy chain having the amino acid sequence of SEQ ID NO: 147; and a light chain having the amino acid sequence of SEQ ID NO: 145;

(jj) a heavy chain having the amino acid sequence of SEQ ID NO: 147; and a light chain having the amino acid sequence of SEQ ID NO: 146;

(kk) a heavy chain having the amino acid sequence of SEQ ID NO: 148; and a light chain having the amino acid sequence of SEQ ID NO: 144;

(ll) a heavy chain having the amino acid sequence of SEQ ID NO: 148; and a light chain having the amino acid sequence of SEQ ID NO: 145;

(mm) a heavy chain having the amino acid sequence of SEQ ID NO: 148; and a light chain having the amino acid sequence of SEQ ID NO: 146;

(nn) a heavy chain having the amino acid sequence of SEQ ID NO: 153; and a light chain having the amino acid sequence of SEQ ID NO: 139;

(oo) a heavy chain having the amino acid sequence of SEQ ID NO: 154; and a light chain having the amino acid sequence of SEQ ID NO: 139; and

(pp) a heavy chain having the amino acid sequence of SEQ ID NO: 155; and a light chain having the amino acid sequence of SEQ ID NO: 139;

wherein the binding protein is a monoclonal antibody.

In another aspect, the invention pertains to a binding protein, e.g., antibody, or antigen binding fragment thereof, capable of binding PRLR that binds to an epitope in PRLR comprising three, four, five, six, seven, eight, nine or all of the amino acid residues E8, F10, C12, R25, E43, G44, I76, D91, E92, L93, Y94, V95, D96, Y99, I100, E145, F160, K185, D187, H188, Y190 and W191 of SEQ ID NO:2. In one embodiment, the binding protein, e.g., antibody, or antigen binding fragment thereof, capable of binding PRLR, binds to an epitope, wherein the epitope comprises at least five of the amino acid residues. In another embodiment, the binding protein, e.g., antibody, or antigen binding fragment thereof, capable of binding PRLR, binds to an epitope, wherein the epitope comprises all of amino acid residues E8, F10, C12, R25, E43, G44, I76, D91, E92, L93, Y94, V95, D96, Y99, I100, E145, F160, K185, D187, H188, Y190 and W191 of SEQ ID NO:2. In a particular embodiment, the binding protein is an antibody, or antigen binding portion thereof, selected from the group consisting of Ab1, Ab6, chAb6, and Ab14-Ab25.

In another aspect, the invention pertains to a binding protein capable of binding PRLR that binds to an epitope in PRLR comprising three, four, five, six, seven, eight, nine or all of the amino acid residues E8, F10, C12, R25, E43, G44, I76, D91, E92, L93, Y94, V95, D96, Y99, I100, E145, F160, K185, D187, H188, Y190 and W191 of SEQ ID NO:2; wherein the binding protein is a monoclonal antibody.

In another aspect, the invention pertains to a binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR that binds to an epitope in PRLR comprising three, four, five, six, seven, eight, nine or all of the amino acid residues E8, I9, F10, K11, C12, R25, E43, G44, W72, T74, I76, D91, E92, L93, Y94, V95, D96, T98, Y99, I100, W139, L143, E145, F160, K185, D187, H188, Y190 and W191 of SEQ ID NO:2. In one embodiment, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR, binds to an epitope, wherein the epitope comprises at least five of the amino acid residues. In another embodiment, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR, binds to an epitope, wherein the epitope comprises all of amino acid residues E8, I9, F10, K11, C12, R25, E43, G44, W72, T74, I76, D91, E92, L93, Y94, V95, D96, T98, Y99, I100, W139, L143, E145, F160, K185, D187, H188, Y190 and W191 of SEQ ID NO:2. In a particular embodiment, the the binding protein is an antibody, or antigen binding portion thereof, selected from the group consisting of Ab4, Ab7, chAb7, Ab35-Ab43 and Ab53-Ab55.

In another aspect, the invention pertains to a binding protein capable of binding PRLR that binds to an epitope in PRLR comprising three, four, five, six, seven, eight, nine or all of the amino acid residues E8, I9, F10, K11, C12, R25, E43, G44, W72, T74, I76, D91, E92, L93, Y94,

V95, D96, T98, Y99, I100, W139, L143, E145, F160, K185, D187, H188, Y190 and W191 of SEQ ID NO:2, wherein the binding protein is a monoclonal antibody.

In another aspect, the invention pertains to a binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR that binds to an epitope in PRLR comprising 13, 14, 15, 16, 17, 18, 19, 20, 21 or all of the amino acid residues R25, T141, L143, E145, R147, E155, W156, E157, I158, H159, F160, A161, G162, Q163, Q164, F167, S171, R183, K185, D187, H188, W191, and W194 of SEQ ID NO:2. In one embodiment, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR, binds to an epitope, wherein the epitope comprises at least 15 of the amino acid residues. In some embodiments, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR, binds to an epitope, wherein the epitope comprises all of amino acid residues R25, T141, L143,

E145, R147, E155, W156, E157, I158, H159, F160, A161, G162, Q163, Q164, F167, S171, R183, K185, D187, H188, W191, and W194 of SEQ ID NO:2. In a particular embodiment, the binding protein is an antibody, or antigen binding portion thereof, selected from the group consisting of Ab3, Ab8, chAb8 and Ab44-Ab52.

In another aspect, the invention pertains to a binding protein capable of binding PRLR that binds to an epitope in PRLR comprising 13, 14, 15, 16, 17, 18, 19, 20, 21 or all of the amino acid residues R25, T141, L143, E145, R147, E155, W156, E157, I158, H159, F160, A161, G162, Q163, Q164, F167, S171, R183, K185, D187, H188, W191 and W194 of SEQ ID NO:2, wherein the binding protein is a monoclonal antibody.

In another aspect, the invention pertains to a binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR that binds to an epitope in PRLR comprising at least one, two, three, four or all of the amino acid residues R25, K185, D187, H188 or W191 of SEQ ID NO:2. In some embodiments, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR, binds to an epitope, wherein the epitope comprises all of amino acid residues R25, K185, D187, H188 or W191 of SEQ ID NO:2. In a particular embodiment, the binding protein is an antibody, or antigen binding portion thereof, selected from the group consisting of Ab1, Ab3, Ab4, Ab6-Ab8, chAb6, chAb7, chAb8, Ab14-Ab25 and Ab35-Ab55.

In another aspect, the invention pertains to a binding protein capable of binding PRLR that binds to an epitope in PRLR comprising at least one, two, three, four or all of the amino acid residues R25, K185, D187, H188 or W191 of SEQ ID NO:2, wherein the binding protein is a monoclonal antibody.

In another aspect, the invention pertains to a binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR that binds to an epitope in PRLR comprising amino acids 91-96 of SEQ ID NO:2. In a particular embodiment, the binding protein is an antibody, or antigen binding portion thereof, selected from the group consisting of Ab1, Ab4, Ab6, Ab7, chAb6, chAb7, Ab14-Ab25, Ab35-Ab43 and Ab53-Ab55.

In another aspect, the invention pertains to a binding protein capable of binding PRLR that binds to an epitope in PRLR comprising amino acids 91-96 of SEQ ID NO:2, wherein the binding protein is a monoclonal antibody.

In another aspect, the invention pertains to a binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR that binds to an epitope having residues within at least amino acids 8-100, 185-191, 8-143, or 183-194 of SEQ ID NO:2. In a particular embodiment, the binding protein is an antibody, or antigen binding portion thereof, selected from the group consisting of Ab1, Ab3, Ab4, Ab6-Ab8, chAb6, chAb7, chAb8, Ab14-Ab25 and Ab35-Ab55.

In another aspect, the invention pertains to a binding protein capable of binding PRLR that binds to an epitope having residues within at least amino acids 8-100, 185-191, 8-143, or 183-194 of SEQ ID NO:2, wherein the binding protein is a monoclonal antibody.

In another aspect, the invention pertains to a binding protein, *e.g.*, antibody, or antigen binding fragment thereof, capable of binding PRLR and having the same epitopic specificity as an antibody, or antigen-binding portion thereof, selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, chAb5, Ab6, chAb6, Ab7, chAb7, Ab8, chAb8, Ab9, chAb9, Ab10, chAb10, Ab11, chAb11, Ab12, chAb12, Ab13, chAb13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab22, Ab23, Ab24, Ab25, Ab26, Ab27, Ab28, Ab29, Ab30, Ab31, Ab32, Ab33, Ab34, Ab35, Ab36, Ab37, Ab38, Ab39, Ab40, Ab41, Ab42, Ab43, Ab44, Ab45, Ab46, Ab47, Ab48, Ab49, Ab50, Ab51, Ab52, Ab53, Ab54 and Ab55.

In another aspect, the invention pertains to a binding protein capable of binding PRLR and having the same epitopic specificity as an antibody, or antigen-binding portion thereof, selected from the group consisting of Ab1, Ab2, Ab3, Ab4, Ab5, chAb5, Ab6, chAb6, Ab7, chAb7, Ab8, chAb8, Ab9, chAb9, Ab10, chAb10, Ab11, chAb11, Ab12, chAb12, Ab13, chAb13, Ab14, Ab15, Ab16, Ab17, Ab18, Ab19, Ab20, Ab21, Ab22, Ab23, Ab24, Ab25, Ab26, Ab27, Ab28, Ab29, Ab30, Ab31, Ab32, Ab33, Ab34, Ab35, Ab36, Ab37, Ab38, Ab39, Ab40, Ab41, Ab42, Ab43, Ab44, Ab45, Ab46, Ab47, Ab48, Ab49, Ab50, Ab51, Ab52, Ab53, Ab54 and Ab55, wherein the binding protein is a monoclonal antibody.

In various embodiments of the foregoing aspects, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, is capable of modulating a biological function of PRLR. In other embodiments of the foregoing aspects, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, binds the ligand binding D1 domain of PRLR. In other embodiments

In another aspect, the invention provides a method for reducing human PRLR activity by contacting human PRLR with a binding protein of the invention, *e.g.*, antibody, or antigen binding fragment thereof, such that human PRLR activity is reduced.

In another aspect, the invention provides a method for reducing human PRLR activity in a human subject suffering from a disorder in which PRLR activity is detrimental, by administering to the human subject a binding protein of the invention, *e.g.*, antibody, or antigen binding fragment thereof, such that human PRLR activity in the human subject is reduced.

In another aspect, the invention provides a method for treating a subject for a disease or a disorder in which PRLR activity is detrimental by administering to the subject a binding protein of the invention, *e.g.*, antibody, or antigen binding fragment thereof, such that treatment is achieved. In one embodiment, the disorder is a cancer. In another embodiment, the cancer is selected from the group consisting of melanoma, endometrial cancer, lymphoma, breast cancer, ovarian cancer, renal carcinoma, gastrointestinal cancer, colon cancer, lung cancer, pancreatic cancer, and prostate cancer. In yet another embodiment, the cancer is breast cancer. In one embodiment, the binding protein, *e.g.*, antibody, or antigen binding fragment thereof, is administered to the subject by at least one mode selected from the group consisting of parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, and transdermal.

In another aspect, the invention provides an anti-PRLR antibody, or antigen binding fragment thereof, that specifically competes with an anti-PRLR binding protein as described herein, wherein said competition can be detected in a competitive binding assay using said antibody, the human PRLR polypeptide, and the anti-PRLR binding protein.

In another aspect, the invention pertains to an anti-PRLR antibody, or antigen binding fragment thereof, that specifically competes with an anti-PRLR binding protein of any one of claims 1-56, wherein said competition can be detected in a competitive binding assay using said antibody, the human PRLR polypeptide, and the anti-PRLR binding protein, wherein the binding protein is a monoclonal antibody.

In another aspect, the invention pertains to an anti-PRLR Antibody Drug Conjugate (ADC) comprising an anti-PRLR antibody, or antigen-binding fragment thereof, and at least one drug, wherein the antibody, or antigen-binding portion thereof, comprises at least 3 CDRs

For example, the invention provides an anti-PRLR Antibody Drug Conjugate (ADC) wherein the antibody, or antigen-binding portion thereof, comprises at least 3 CDRs selected from a heavy chain variable domain CDR set (CDR1, CDR2, and CDR3) consisting of SEQ ID NOs: 40, 41, and 42; SEQ ID NOs: 46, 47, and 42; SEQ ID NOs: 56, 57, and 58; SEQ ID NOs: 62, 63, and 58; SEQ ID NOs: 71, 72, and 73; SEQ ID NOs: 71, 77, and 73; SEQ ID NOs: 85, 86, and 87; SEQ ID NOs: 149, 150, and 87. Alternatively or in combination, the invention provides an anti-PRLR Antibody Drug Conjugate (ADC) wherein the antibody, or antigen-binding portion

Dacarbazine (DTIC), chlorambucil, melphalan, carboplatin, oxaliplatin, doxorubicin HCL, daunorubicin citrate, mitoxantrone HCL, actinomycin D, etoposide, topotecan HCl, teniposide, irinotecan HCL(CPT-ll), vincristine, vinblastine sulfate, vinorelbine tartrate, vindesine sulphate, paclitaxel, docetaxel, abraxane, ixabepilone, imatinib mesylate, sunitinib malate, sorafenib toslate, nilotinib hydrochloride monohydrate, L-asparaginase, alpha interferon, Avastin, IL-2, Aldesleukin, Proleukin, IL-12, Toremifene citrate, Fulvestrant, raloxifene HCL, anastrazole, letrozole, Fadrozole (CGS 16949A), exemestane, leuprolide acetate, Lupron, goserelin acetate, triptorelin pamoate, buserelin, Nafarelin, cetrorelix, bicalutamide, nilutamide, megestrol acetate, somatostatin Analogs, prendinsolone, dexamethasone, ketoconazole, sirolimus, temsirolimus (CCI-779), deforolimus (AP23573), and everolimus (RAD00I).

In another aspect, the invention pertains to a pharmaceutical composition comprising an ADC as described above.

In yet another aspect, the invention pertains to a method of treating cancer in a subject in need thereof, said method comprising administering an ADC as described above, such that the subject is treated.

In another aspect, the invention pertains to a method of treating cancer in a subject in need thereof, said method comprising administering an ADC as described above, such that the subject is treated, wherein the cancer is selected from the group consisting of melanoma, endometrial cancer, lymphoma, breast cancer, ovarian cancer, renal carcinoma, gastrointestinal cancer, colon cancer, lung cancer, pancreatic cancer, and prostate cancer. In other embodiments, the invention pertains to to a method of treating cancer in a subject in need thereof, said method comprising administering an ADC as described above, such that the subject is treated, wherein the cancer is breast cancer. In other embodiments, the invention pertains to to a method of treating cancer in a subject in need thereof, said method comprising administering an ADC as described above, such that the subject is treated, wherein the ADC is administered to the subject by a mode selected from the group consisting of parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, and transdermal.

In another aspect, the invention pertains to the use of an effective amount of the composition as disclosed herein in the manufacture of a medicament for treating a mammal.

In another aspect, the invention pertains to the use of the binding protein as disclosed herein in the manufacture of a medicament for reducing human PRLR, wherein human PRLR is to be contacted with the medicament such that human PRLR activity is reduced.

In another aspect, the invention pertains to the use of the binding protein as disclosed herein in the manufacture of a medicament for reducing human PRLR activity in a human subject suffering from a disorder in which PRLR activity is detrimental, wherein the medicament is to be administered to the human subject such that human PRLR activity in the human subject is reduced.

In another aspect, the invention pertains to the use of the subject the binding protein as disclosed herein in the manufacture of a medicament for treating a subject for a disease or a disorder in which PRLR activity is detrimental, wherein the medicament is to be administered to the subject, such that treatment is achieved.

In another aspect, the invention pertains to the use of the ADC as disclosed herein in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the medicament is to be administered, such that the subject is treated.

83. A method of producing a protein capable of binding PRLR, comprising culturing a host cell of any one of claims 76-82 in culture medium under conditions sufficient to produce a binding protein capable of binding PRLR.

84. A protein produced according to the method of claim 83.

85. A composition for the release of a binding protein said composition comprising:
(a) a formulation, wherein said formulation comprises a crystallized binding protein, according to claim 67, and an ingredient; and
(b) at least one polymeric carrier.

86. The composition according to claim 85, wherein said polymeric carrier is a polymer selected from one or more of the group consisting of: poly (acrylic acid), poly (cyanoacrylates), poly (amino acids), poly (anhydrides), poly (depsipeptide), poly (esters), poly (lactic acid), poly (lactic-co-glycolic acid) or PLGA, poly (b-hydroxybutryate), poly (caprolactone), poly (dioxanone); poly (ethylene glycol), poly ((hydroxypropyl) methacrylamide, poly [(organo) phosphazene], poly (ortho esters), poly (vinyl alcohol), poly (vinylpyrrolidone), maleic anhydride- alkyl vinyl ether copolymers, pluronic polyols, albumin, alginate, cellulose and cellulose derivatives, collagen, fibrin, gelatin, hyaluronic acid, oligosaccharides, glycaminoglycans, sulfated polysaccharides, blends and copolymers thereof.

87. The composition according to claim 85 or 86, wherein said ingredient is selected from the group consisting of albumin, sucrose, trehalose, lactitol, gelatin, hydroxypropyl-β-cyclodextrin, methoxypolyethylene glycol and polyethylene glycol.

88. ~~A method for treating a mammal comprising the step of administering to the mammal~~ Use of an effective amount of the composition according to any one of claims 85-87 in the manufacture of a medicament for treating a mammal.

89. A pharmaceutical composition comprising the binding protein of any one of claims 1-56, and a pharmaceutically acceptable carrier.

90. The pharmaceutical composition of claim 89 wherein said pharmaceutically acceptable carrier functions as adjuvant useful to increase the absorption, or dispersion of said binding protein.

91. The pharmaceutical composition of claim 90 wherein said adjuvant is hyaluronidase.

92. The pharmaceutical composition of any one of claims 89-91 further comprising at least one additional therapeutic agent for treating a disorder in which PRLR activity is detrimental.

93. The pharmaceutical composition of claim 92, wherein said additional agent is selected from the group consisting of: therapeutic agent, imaging agent, cytotoxic agent, angiogenesis inhibitors; kinase inhibitors; co-stimulation molecule blockers; adhesion molecule blockers; anti-cytokine antibody or functional fragment thereof; methotrexate; cyclosporin; rapamycin; FK506; detectable label or reporter; a TNF antagonist; an anti-rheumatic; a muscle relaxant, a narcotic, a non-steroid anti-inflammatory drug (NSAID), an analgesic, an anesthetic, a sedative, a local anesthetic, a neuromuscular blocker, an antimicrobial, an antipsoriatic, a corticosteriod, an anabolic steroid, an erythropoietin, an immunization, an immunoglobulin, an immunosuppressive, a growth hormone, a hormone replacement drug, a radiopharmaceutical, an antidepressant, an antipsychotic, a stimulant, an asthma medication, a beta agonist, an inhaled steroid, an oral steroid, an epinephrine or analog, a cytokine, and a cytokine antagonist.

94. ~~A method for reducing human PRLR activity comprising contacting human PRLR with~~ Use of the binding protein of any one of claims 1-56 in the manufacture of a medicament for reducing human PRLR, wherein human PRLR is to be contacted with the medicament such that human PRLR activity is reduced.

95. ~~A method for reducing human PRLR activity in a human subject suffering from a disorder in which PRLR activity is detrimental, comprising administering to the human subject~~ Use of the binding protein of any one of claims 1-56 in the manufacture of a medicament for reducing human PRLR activity in a human subject suffering from a disorder in which PRLR activity is detrimental, wherein the medicament is to be administered to the human subject such that human PRLR activity in the human subject is reduced.

96. ~~A method for treating a subject for a disease or a disorder in which PRLR activity is detrimental by administering to~~ Use of the subject the binding protein of any one of claims 1-56 in the manufacture of a medicament for treating a subject for a disease or a disorder in which PRLR activity is detrimental, wherein the medicament is to be administered to the subject, such that treatment is achieved.

97. The ~~method~~ use of claim 96, wherein the disorder is a cancer.

98. The ~~method~~ use of claim 97, wherein the cancer is selected from the group consisting of melanoma, endometrial cancer, lymphoma, breast cancer, ovarian cancer, renal carcinoma, gastrointestinal cancer, colon cancer, lung cancer, pancreatic cancer, and prostate cancer.

99. The ~~method~~ use of claim 97, wherein the cancer is breast cancer.

100. The ~~method~~ use according to any one of claims 96-99, wherein said ~~binding protein~~medicament is to be administered to the subject by a mode selected from the group consisting of parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, and transdermal.

101. An anti-PRLR antibody, or antigen binding fragment thereof, that specifically competes with an anti-PRLR binding protein of any one of claims 1-56, wherein said competition can be detected in a competitive binding assay using said antibody, the human PRLR polypeptide, and the anti-PRLR binding protein, wherein the binding protein is a monoclonal antibody.

102. An anti-PRLR Antibody Drug Conjugate (ADC) comprising an anti-PRLR antibody, or antigen-binding fragment thereof, and at least one drug, wherein the antibody, or antigen-binding portion thereof, comprises at least 3 CDRs.

irinotecan HCL(CPT-ll), vincristine, vinblastine sulfate, vinorelbine tartrate, vindesine sulphate, paclitaxel, docetaxel, abraxane, ixabepilone, imatinib mesylate, sunitinib malate, sorafenib toslate, nilotinib hydrochloride monohydrate, L-asparaginase, alpha interferon, Avastin, IL-2, Aldesleukin, Proleukin, IL-12, Toremifene citrate, Fulvestrant, raloxifene HCL, anastrazole, letrozole, Fadrozole (CGS 16949A), exemestane, leuprolide acetate, Lupron, goserelin acetate, triptorelin pamoate, buserelin, Nafarelin, cetrorelix, bicalutamide, nilutamide, megestrol acetate, somatostatin Analogs, prendinsolone, dexamethasone, ketoconazole, sirolimus, temsirolimus (CCI-779), deforolimus (AP23573), and everolimus (RAD00I).

107. A pharmaceutical composition comprising the ADC of any one of claims 102-106.

108. ~~A method of treating cancer in a subject in need thereof, said method comprising administering~~ Use of the ADC of any one of claims 102-107 in the manufacture of a medicament for treating cancer in a subject in need thereof, wherein the medicament is to be administered, such that the subject is treated.

109. The ~~method~~ use of claim 108, wherein the cancer is selected from the group consisting of melanoma, endometrial cancer, lymphoma, breast cancer, ovarian cancer, renal carcinoma, gastrointestinal cancer, colon cancer, lung cancer, pancreatic cancer, and prostate cancer.

110. The ~~method~~ use of claim 108, wherein the cancer is breast cancer.

111. The ~~method~~ use according to any one of claims 108-110, wherein the ~~ADC~~ medicament is administered to the subject by a mode selected from the group consisting of parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracerebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, and transdermal.