Supplementary Table 1: USPTO Patent and Patent Applications Ligand and Receptor Interface P/PA

| Compound/Category | Title or Example Thereof for Multiple Patents | Inhibitor or | Molecular | Assignee | Patents and/or Patent |
|---------------------|---|--------------|--|---|---|
| | | Enhancer | target | | Applications |
| Dkk protein | Therapeutic implications of dickkopf affecting cancer stem cell fate | Inhibition | LRP5/6 | Institute for Medical Biomathematics | 8762069 |
| Dkk protein | Use of WNT inhibitors to augment therapeutic index of chemotherapy | Inhibition | LRP5/6 | The Board of Trustees of the Leland Stanford Junior University | 7803783 |
| Dkk protein | Human Zven1 DNA, Peptides and polypeptides and Antibodies that bind human Zven1 | Inhibition | Wnt ligands | ZymoGenetics Inc | 6485938, 6756479, 6828425, 7122349, 7179787, 7662641, 7691585, 7691610, |
| Dkk genes | Inhibitor protein of the wnt signal pathway | Inhibition | Wnt ligands/ LRP5/6 receptor | Deutsches Krebsforschungszentrum Stiftung des Offentlichen Rechts | 6844422, 7138508, 8461309, 8536311 |
| DKK inhibitor | Composition of tumor-associated peptides and related anti- cancer vaccine for the treatment of glioblastoma (GBM) and other cancers | | 8895514, 8653035, 8961985, 20150125478, | | |
| Dkk protein | Prokaryotic expression of soluble, active Dkk | Inhibition | LRP5/6 | St. Jude Children's Hospital | 8470554 |
| Dkk protein | Human dickkopf-related protein and nucleic acid molecules and uses therefor | Inhibition | Wnt ligands/ LRP5/6 receptor | Millennium Pharmaceuticals | 7057017, 7579168, 7645451, 8202966, 20100093978 |
| Dkk1 protein | WNT FAMILY-DERIVED PEPTIDES AND USE THEREOF | Inhibition | LRP5/6 | CAREGEN CO., LTD. | 20140309157 |
| Dkk1 protein | METHOD FOR PREPARING INDUCED PARAXIAL MESODERM PROGENITOR (IPAM) CELLS AND THEIR USE | Inhibition | LRP5/6 | INSERM, ASSOCIATION FRANCAISE CONTRE LES MYOPATHIES, UNIVERSITE DE STRASBOURG, CNRS | 20140363886 |
| DKK1 protein | METHOD FOR FORMING ENDOTHELIAL CELLS | Inhibition | LRP5/6 | Korea Advanced Institute of Science and Technology (KAIST) | 20150368617 |
| Dkk1 and Dkk3 dsRNA | Compositions and methods for inhibiting cell migration | Enhancer | Dkk1/3 | The Burnham Institute | 7833980, 8039255 |
| Dkk1 Antagonist | Inhibitors of Dkk-1 | Enhancer | Dkk1 | Administrators of the Tulane Educational Fund | 20080085281 |
| DKK1 antibody | Use of Anti-DKK-1 Monoclonal Antibodies for the Treatment of Liver Cancer | Enhancer | Dkk-1 | | 20120201810 |

| Compound/Category | Title or Example Thereof for Multiple Patents | Inhibitor or Enhancer | Molecular target | Assignee | Patents and/or Patent Applications |
|---|--|--------------------------|---------------------|---|------------------------------------|
| DKK1 antibody | DKK1 ANTIBODIES AND METHODS OF USE | Enhancer | Dkk-1 | | 20130209475 |
| DKK1 antibody | Antibodies to Dkk-1 | Enhancer | Dkk1 | Amgen | 7709611 |
| DKK1 antibody | Treatment involving Dkk-1 or antagonists thereof | Enhancer | Dkk1 | Genetech, Inc. | 20030165501 |
| DKK1 antibody | antibody Antibodies that bind human Dickkopf-1 proteins | | Dkk1 | Millennium Pharmaceuticals | 7446181, 20100093056 |
| DKK1 antibody | Antibodies specific for Dkk-1 | | Dkk1 | Merck Sharp & Dohme Corp. | 7994293 |
| DKK1 antibody and over- expression of Wnt-3a | Overexpression of Wnt ligands and treatment of lytic bone diseases | Enhancer | Dkk1/wnt3-a | The Board of Trustees of the University of Arkansas | 8501702 |
| Dkk1 fragment | Compositions and methods for inhibiting cell migration | Enhancer | Dkk1 | The Burnham Institute | 7465585 |
| DKK1 protein | INHIBITION OF HAIR FOLLICLE GROWTH BY THE WNT INHIBITOR DKK1 | Inhibition | LRP5/6 | | 20120165270 |
| Dkk1 protein | Differentiation of human embryonic stem cells | Inhibition | LRP5/6 | LifeScan, Inc. | 9096832 |
| DKK1 protein | Molecules, Compositions and Methods to Treat Organ Scarring | Inhibition | LRP5/6 | | 20150337021 |
| DKK1 shRNA or siRNA | shRNA Materials and Methods of Using Same for Inhibition of DKK-1 | Enhancer | Dkk1 | The Regents of the University of Michigan | 20080293053 |
| Dkk1, Dkk2 protein | NOVEL METHODS TO REGENERATE HUMAN LIMBAL STEM CELLS | Inhibition | LRP5/6 | THE REGENTS OF THE UNIVERSITY OF CALIFORNIA | 20150175965 |
| Frizzled 7 expression | Frizzled proteins and detection and treatment of cancer | Inhibition | Frizzled-7 | Rhode Island Hospital | 7867705 |

| Compound/Category | Title or Example Thereof for Multiple Patents | Inhibitor or Enhancer | Molecular target | Assignee | Patents and/or Patent Applications |
|---|--|--------------------------|--|---|---|
| Frizzled antibody (OMP- 18R5) and Soluble Frizzed8 | Combination Therapy for Treatment of Cancer | Inhibition | Receptor | | 20150132301 |
| Frizzled antibody or polypeptide or lipid or small molecule | Frizzled-binding agents and their use in screening for WNT inhibitors | Inhibition | Frizzled | OncoMed Pharmaceuticals Inc. | 8551789, 7982013, 8507442, 9168300, 20140242078 |
| Frizzled, Soluble | Wnt antagonists and their use in the diagnosis and treatment of Wnt-mediated disorders | Inhibition | bition Wnt Genentech Inc. | | 7947277 |
| Frizzled, Soluble | Use of FZC18-Containing Collagen 18 Polypeptides for the Treatment, Diagnosis and Outcome Prediction of Diseases | Inhibition | Wnt ligands | INSERM, Paris | 20100316616 |
| Frizzled, Soluble | led, Soluble Wnt antagonists and methods of treatment and screening | | Wnt ligands and Frizzled receptors | OncoMed Pharmaceuticals Inc. | 9157904 |
| Frizzled, Soluble (FRP) | Human FRP and fragments thereof including methods for using them | Inhibition | Wnt ligands | USA dept Health and Human Services | 7183377 |
| Frizzled, Soluble (FRP) | Polynucleotides encoding human FRP and fragments thereof | Inhibition | Wnt ligands | USA dept Health and Human Services | 6479255 |
| Frizzled, Soluble (Frzb) | Method of modulating tissue growth using Frzb Protein | Inhibition | Wnt ligands | USA dept Health and Human Services | 6924367, 7049291, 7563596 |
| Frizzled, Soluble (sFRP- 1) | Differentiation of stem cells into dopaminergic cells | Inhibition | Frizzled | The United States of America, as represented by the Secretary, Department of Health and Human | 8628962 |
| Frizzled10 antibodies | Anti-FZD10 monoclonal antibodies and methods for their use | Inhibition | Frizzled-10 | Omeros Corporation | 9102724 |
| Frizzled3/8/9 antibodies and sFRP1/2/3 | METHODS AND COMPOSITIONS FOR NERVE REGENERATION | Inhibition | Frizzled-3/8/9 | The University of Chicago | 20080299135 |
| Frizzled7 antibodies | Wnt proteins and detection and treatment of cancer | Inhibition | Frizzled-7 | Rhode Island Hospital | 8158761 |
| LPR5/6 Receptor antagonist (Apcdd peptide) | Use of WNT inhibitor to inhibit angiogenesis in the CNS | Inhibition | LRP5 and Wnt3a | | 20110189097 |

| Compound/Category | Title or Example Thereof for Multiple Patents | Inhibitor or Enhancer | Molecular target | Assignee | Patents and/or Patent Applications |
|-------------------------|---|--------------------------|---------------------|--|--|
| LRP5/6 and Dkk proteins | Compounds and assays for controlling Wnt activity | Inhibition | LRP5/6 and Dkk | Enzo Biochem, Inc. | 9052324 |
| LRP5/6 antibody | Methods of using an antibody to inhibit WNT-mediated cardiac remodeling | Inhibition | LRP5/6 | Vanderbilt University | 8790650, 9175090, 9303087 |
| LRP5/6 antibody | Antibodies That Inhibit WNT Signaling and Methods of Using The Same | Inhibition | LRP5/6 | | 20120276089 |
| LRP6 antibody | Anti-LRP6 antibodies | Inhibition | LRP6 | Genentech, Inc. | 8846041 |
| LRP6 antibody | MOLECULES AND METHODS FOR MODULATING LOW-DENSIT LIPOPROTEIN RECEPTOR-RELATED PROTEIN 6 (LRP6) | | LRP6 | Novartis | 20100254980 |
| LRP6 antibody | Monoclonal antibodies that inhibit the wnt signaling pathway and methods of production and use thereof | Inhibition | LRP6 | The Board of Regents of the University of Oklahoma | 20120045437 |
| RSPO 1 protein | COMPOSITIONS AND METHODS RELATING TO INDUCTION OF INTESTINAL STEM CELL HOMEOGENESIS AND/OR REGENERATION | Enhancer | ligand- Receptor | The Regents of the University of Michigan | 20160000865 |
| RSPO Antibody | Anti-RSPO1 antibodies | Inhibition | RSPO1 | Genentech, Inc. | 8802097 |
| SOST antibody | Antibodies that specifically bind SOST peptides | Enhancer | SOST | Stowers Institute for Medical Research | 7893218, 7968301, 8168761, 8173125, 8546545, 9321835 |
| Tiki 1/2 antibodies | Tiki1 and Tiki2, Wnt Inhibitors | Enhancer | Tiki1 and Tiki2 | Children's Medical Center Corp. | 20130101582 |
| Wnt 7a/b proteins | WNT LIGANDS INVOLVED IN BLOOD-BRAIN BARRIER DEVELOPMENT AND USES THEREFOF | Enhancer | Frizzled | President and Fellows of Harvard College | 20100199362 |
| Wnt antibody | Wnt and frizzled receptors as targets for immunotherapy in head and neck squamous cell carcinomas | Inhibition | Wnt1 | University of California Oakland | 7682607 |
| Wnt antibody | Wnt and frizzled receptors as targets for immunotherapy in head and neck squamous cell carcinomas | Inhibition | Wnt14 | University of California Oakland | 7713526 |

| Compound/Category | Title or Example Thereof for Multiple Patents | Inhibitor or Enhancer | Molecular target | Assignee | Patents and/or Patent Applications |
|-----------------------------------|---|----------------------------|---|---|------------------------------------|
| Wnt antibody | METHODS FOR TREATING CANCER BY INHIBITING WNT SIGNALING | Inhibition | Wnt1 | Regents of the University of California, Oakland | 20090304695 |
| Wnt antibody | WNT-Binding Agents and Uses Thereof | | Wnt1,2,2b,3,3 OncoMed Pharmaceuticals Inc. a,7a,7b,8a,8b, 10a and 10b | | 20130045209 |
| Wnt antibody | Mammalian Wnt polypeptide-5 | inhibition | Wnt5 | ZymoGenetics Inc | 20030017980 |
| Wnt inhibiton polypeptide | NON-ACTIVATED WNT INHIBITION POLYPEPTIDES AND METHOD Inhibition Wnt ligand FOR PREPARING THE SAME (Mini- WNT COMPOSITIONS AND METHODS OF USE THEREOF Inhibition Frizzled and The Board of Trustees of the Leland | | 20090325866 | | |
| Wnt polypeptides (Mini- Wnt | nt polypeptides (Mini- nt | | Frizzled and LRP5/6 | The Board of Trustees of the Leland Stanford Junior University | 20140200179 |
| Wnt protein | tein Use of Wnt Agents to Prevent Hypoxic Injury Enhancer Frizzle | | Frizzled | The Board of Trustees of the Leland Stanford Junior University | 20140141061 |
| Wnt receptor decoy (sLRP6E1E2) | ANTI-CANCER COMPOSITIONS CONTAINING WNT DECOY RECEPTOR | Inhibition | Wnt ligand | INDUSTRY-UNIVERSITY COOPERATION FOUNDATION HANYANG UNIVERSITY | 20140315825 |
| Wnt-10 protein | WNT10-derived peptide and use thereof | Enhancer | Frizzled | Caregen Co., Ltd. | 8497241 |
| Wnt-5a peptide | Peptide ligand to impair cancer cell migration | Inhibition of Canonical | Receptor | Wntresearch AB | 8674060 |
| Wnt-Fzd chimera | Wnt-frizzled chimera | Enhancer | Pathway activation | Wyeth | 20070072238 |
| Wnt1/2/3a meroduplex RNA | NUCLEIC ACID COMPOUNDS FOR INHIBITING WNT GENE EXPRESSION AND USES THEREOF | Inhibition | Wnt1/2/3A | MDRNA, Inc | 20100055784 |
| Wnt3A protein | Use of liposomal Wnt composition to enhance osseointegration | Enhancer | Frizzled and LRP5/6 | The Board of Trustees of the Leland Stanford Junior University | 8809272 |
| Wnt3A protein | Methods of promoting cardiac cell proliferation | Enhancer | Frizzled | Hydra | 20050261189 |

| Compound/Category | Title or Example Thereof for Multiple Patents | Inhibitor or | Molecular | Assignee | Patents and/or Patent |
|-------------------|--|--------------|--------------|---------------------------|--------------------------|
| | | Enhancer | target | | Applications |
| Wnt4a protein | HLDAT86 polynucleotides | not | Frizzled | SmithKline Beecham P.L.C. | 6165751 |
| | | specified | receptors | | |
| | | | | | |
| Wnt7a polypeptide | | Enhancer | Frizzled and | Fate Therapeutics Inc | 20150099708, 20140142046 |
| | WNT COMPOSITIONS AND THERAPEUTIC USES OF SUCH | | LRP5/6 | | |
| | COMPOSITIONS | | | | |
| Wnt7a protein | COMPOSITIONS, METHODS AND KITS FOR DETECTING AND | Inhibition | Frizzled | University of Miami | 20110039788 |
| | TREATING CANCER | | | | |
| | | | | | |

Supplementary Table 1: USPTO Patent and Patent Applications beta-catenin P/PA

| Compound/Category | Title or Example Thereof for Multiple Patents | Inhibitor or Enhancer | Molecular target | Biomolecule or Chemical | Assignee | Patents and/or Patent Applications |
|---|--|---------------------------|---------------------------------------|----------------------------|---|---|
| bc19 like protein w/ mutations | .betacatenin nuclear localized protein | Inhibition | β-catenin | Biomolecule | Kyowa Hakko Kogyo Co | 7358348 |
| BCL9 HD2 helix | TARGETING DEREGULATED WNT SIGNALING IN CANCER USING STABILIZED ALPHA-HELICES OF BCL-9 | Inhibition | β-catenin | Biomolecule | Dana-Farber Cancer Institute Inc. | 20140113857 |
| compound | Compounds useful for treatment of cancer, compositions containing the same, and methods of their use | Inhibition | β-catenin-TCF4 -CBP complex | Chemical | Choongwae Pharma Corp | 6762185 |
| debromohymenialdesine (dBHD) and dBHD analogs | Wnt signaling inhibitors, and methods for making and using them | Inhibition | β-catenin-TCF complex | Chemical | The Regents of the University of California | 8304408 |
| disulfonamide derivatives | Derivatives of fluorene, anthracene, xanthene, dibenzosuberone and acridine and uses thereof | Inhibition | β-catenin | Chemical | Dogwood Pharmaceuticals, Inc. | 8129519, 9120754 |
| Dvl, Wnt, phosphatase PP2A, CKI7, phosphatase inhibitors, FRAT1 | Methods and compositions for modulating beta-catenin phosphorylation | Enhancer or Inhibition | β-catenin phosphorylation on Ser45 | Biomolecule | | 20050171005 |
| GSK3 inhibitor | ACTIVATED WNT-BETA-CATENIN SIGNALING IN MELANOMA | Enhancer | β-catenin | Chemical | Yale University & University of Washington | 20110293750 |
| LXXLL peptide | Compounds and methods for modulating .betacatenin mediated gene expression | Inhibition | β-catenin | Biomolecule | Adherex Technologies | 6677116, 6303576 |
| methods to modulate Fbp1 activity | NOVEL UBIQUITIN LIGASES AS THERAPEUTIC TARGETS | Inhibition | β-catenin | Biomolecule | New York University | 20090104642, 20050079558 |
| Nefopam | Method of treating scars and .betacatenin-mediated disorders using Nefopam compounds | Inhibition | β-catenin | Chemical | The Hospital for Sick Children | 8957107 |
| non-peptide reverse-turn mimics | Reverse-turn mimetics and method relating thereto | Inhibition | β-catenin-TCF4 -CBP complex | Chemical | Choongwae Pharma Corp. | 8049008, 8729262, 8138337, 8318738, 7932384, 8101751, 8106049, 7232822, 7566711, 7576084, 7585862, 7671054 |
| oligomers (w specific formulas) | Compounds for the modulation of beta-catenin expression | Inhibition | β-catenin mRNA | Biomolecule | Enzon Pharmaceuticals Inc. and Santaris Pharma | 7915401, 8039446 |
| Oxazole and thiazole small molecules | Oxazole and thiazole compounds as beta-catenin modulators and uses thereof | Inhibition | β-catenin | Chemical | New York University | 9173871, 8252823 |
| peptides that bind β- catenin such as cadherins | Methods and therapeutic compositions for treating cancer | inhibition | β-catenin | Biomolecule | 2002 | 20020045591 |
| peptidomimetic macrocycle (contains a helix) | PEPTIDOMIMETIC MACROCYCLES | Inhibition | β-catenin-TCF4 -CBP complex | Biomolecule | | 20130072439 |

| Compound/Category | Title or Example Thereof for Multiple Patents | Inhibitor or Enhancer | Molecular target | Biomolecule or Chemical | Assignee | Patents and/or Patent Applications |
|-----------------------------------|---|--------------------------|-------------------------|----------------------------|---|------------------------------------|
| quinazoline derivatives | AMINO-SUBSTITUTED QUINAZOLINE DERIVATIVES AS INHIBITORS OF BETA-CATENIN/TCF-4 PATHWAY AND CANCER TREATMENT AGENTS | Inhibition | β-catenin-TCF complex | Chemical | Wyeth | 20090004185 |
| RNAi agent | ORGANIC COMPOSITIONS TO TREAT BETA-CATENIN- RELATED DISEASES | Inhibition | β-catenin | Biomolecule | NOVARTIS AG | 20150291954 |
| RXR agonist | Methods and compositions for the treatment of cancer | Inhibition | β-catenin | Chemical | Allergan | 20040009921 |
| SIRT1 levels or activity | L levels or activity SIRTUIN BASED METHODS AND COMPOSITIONS FOR TREATING BETA-CATENIN-RELATED CONDITIONS | | β-catenin deacetylation | Biomolecule | President and Fellows of Harvard College | 20110009474 |
| small molecule | CBP/CATENIN ANTAGONISTS FOR ENHANCING ASYMMETRIC DIVISION OF SOMATIC STEM CELLS | Inhibition | β-catenin-CBP | Chemical | University of Southern California | 20150232468 |
| small molecules | INHIBITORS OF BETA-CATENIN IN TREATMENT OF COLORECTAL CANCER | Inhibition | β-catenin-TCF4 complex | Chemical | | 20150374662 |
| stapled alpha-helical peptides | Beta-catenin targeting peptides and uses thereof | Inhibition | β-catenin | Biomolecule | President and Fellows of Harvard College | 8957026 |
| TRPV4 inhibitor | PROTEIN INVOLVED IN DETECTION OF CANCER METASTASIS AND A TREATMENT THEREOF | Enhancer | β-catenin-E-cadherin | Chemical | National University of Singapore | 20140199330 |
| 3-catenin peptides | Agents for treating human illnesses based on .betacatenin, and the production and use thereof | Inhibition | β-catenin-TCF complex | Biomolecule | Max-Delbruck-Centrum fur Molekulare Medizin | 7067474 |
| 3-catenin protein | Methods for generating new hair follicles, treating baldness, and hair removal | Enhancer | β-catenin | Biomolecule | The Trustees of the University of Pennsylvania | 9220926 |

Supplementary Table 1: USPTO Patent and Patent Applications All others P/PA

| Compound/Category | Title | Inhibitor or Enhancer | Molecular target | Interaction at level of: | Assignee | Patents and/or Patent Applications |
|---|---|--------------------------|--|--------------------------|--|------------------------------------|
| Tankerase inhibitors | 2-piperidin-1-yl-acetamide compounds for use as tankyrase inhibitors | Inhibition | Axin1/2 via tankerase | Axin1/2 | Novartis | 9181266, 9227982 |
| Tankerase inhibitors | 4-piperidinyl compounds for use as tankyrase inhibitors | Inhibition | Axin1/2 via tankerase | Axin1/2 | Novartis AG | 9163003 |
| small molecule inhibitor | 3-aryl-5-substituted-isoquinolin-1-one compounds and their therapeutic use | Inhibition | PARP1, TNKS1, TNKS2, etc | Axin1/2 | Insititute of cancer research: Royal Cancer Hospital | 9193689 |
| small molecule inhibitor | Pyrvinium For The Treatment of Cancer | Inhibition | Pyrvinium | Axin1/2 | | 20090099062 |
| Azole derivatives | Azole derivatives as WTN pathway inhibitors | Inhibition | stabilize Axin2/destruction complex | Axin1/2 | Oslo University Hospital HF | 8883827, 9096587 |
| nucleic acid, fushion protein, compound | METHODS AND COMPOSITIONS FOR MEASURING WNT ACTIVATION AND FOR TREATING WNT-RELATED CANCERS | Inhibition | Tankyrase-Axin | Axin1/2 | Novartis | 20100267626 |
| Casein kinase inhibitors | BIFLUORODIOXALANE-AMINO-BENZIMIDAZOLE KINASE INHIBITORS FOR THE TREATMENT OF CANCER, AUTOIMMUNEINFLAMMATION AND CNS DISORDERS | Inhibition | Casein kinase 1 family | Casein Kinase 1 | 4SC DISCOVERY GMBH | 20150158878 |
| CKI polypeptides | Compositions and methods of diagnosis and treatment using casein kinase I | Inhibition | Wnt pathway | Casein Kinase 1 | Chiron Corporation | 6512102 |
| DACT3, Wnt ligand inhibitors (Dkk-1, WIF-1, SFRPs) | Methods and compounds for preventing and treating a tumour | Inhibition | DACT3: Dvl2, | Dishevelled | Agency for Science, Technology and Research | 8969313 |
| 6-bromo-indirubin (BIO), 5-amino- indirubin and N-methyl-indirubins and related indirubin derivatives | Indirubin-Type Compounds, Compositions, and Methods for Their Use | Enhancer | GSK3, CDKs, aryl hydorcarbon recpetors | GSK3 | | 20070276025 |

Supplementary Table 2: Clincal Trials

| Number | Identifier | Sponsor | Date Received | Condition | Intervention | target/method | Aliases | <u>Status</u> | Inhibition/A | <u>Phase</u> |
|--------|-------------|--|---------------|---|----------------------------------|--------------------------------|------------------------------------|-----------------|--------------------------|---------------------|
| | | | | | | of action | | | ctivation | |
| 1 | NCT02278133 | Array BioPharma | 06-Oct-14 | Metastatic CRC | Wnt974 | Porcupine | | recruiting | Inhibtion | Phase 1 Phase 2 |
| 2 | NCT02649530 | University of Michigan Cancer Center | 05-Jan-16 | Squamous Cell Carcinoma, Head And Neck | Wnt974 | Porcupine | | Not yet open | Inhibtion | Phase 2 |
| 3 | NCT01351103 | Novartis Pharmaceuticals | 04-May-11 | Pancreatic Adenocarcinoma; BRAF Mutant Colorectal Cancer; Other Tumor Types With Documented Genetic Alterations Upstream in the Wnt Signaling Pathway | LGK974 | Porcupine | | Suspended | Inhibtion | Phase 1 |
| 4 | NCT02413853 | University of Southern California | 07-Apr-15 | Metastatic CRC | PRI-724 | CBP/β-catenin | | not yet open | Inhibtion | Phase 2 |
| 5 | NCT01323894 | China Medical University Hospital | 24-Mar-11 | Primary Disease (Osteoporosis*) | Wnt3a | Activation of Wnt/β-catenin | | Unknown | Activation | ? |
| 6 | NCT02020291 | WntResearch AB | 11-Dec-13 | Metastatic Breast Cancer; CRC; Prostate Cancer | Foxy-5 | Frizzled receptor | Wnt5a mimic | completed | Inhibition of metastases | Phase 1 |
| 7 | NCT01548066 | Seoul National University Hospital | 20-Jul-11 | Androgenetic Alopecia; Male Pattern Baldness | Valproic Acid | GSK3b | Depakene | completed | Activation | Phase 2 |
| 8 | NCT01764477 | Prism Pharma Co., Ltd. | 12-Dec-12 | Pancreatic Adenocarcinoma | PRI-724 | CBP/β-catenin | | completed | Inhibition | Phase 1 |
| 9 | NCT02655952 | WntResearch AB | 06-Jan-16 | Metastatic: Breast, Colon, Prostate Cancer | Foxy-5 | Frizzled receptor | Wnt5a mimic | not yet open | Inhibition of metastases | Phase 1b |
| 10 | NCT01398462 | JW Pharmaceutical | 17-Jul-11 | Acute Myeloid Leukemia | CWP232291 | β-catenin | | completed | Inhibition | Phase 1 |
| 11 | NCT02029352 | Maastricht University Medical Center | 18-Dec-13 | Basal Cell Carcinoma | Topical Green Tea Ointment | Unspecified | epigallocat echin-3- gallate | completed | inhibition | Phase 2, Phase 3 |

| Number | <u>Identifier</u> | Sponsor | Date Received | Condition | Intervention | target/method | Aliases | <u>Status</u> | Inhibition/A | <u>Phase</u> |
|--------|-------------------|--|---------------|---|----------------------|--|------------------------|---------------|--------------|--------------------|
| | | | | | | of action | | | ctivation | |
| 12 | NCT02687009 | Michael Morse, | 10-Feb-16 | Colon Cancer | Niclosamide | Frizzled | Yomensan | not yet | Inhibition | Phase 1 |
| | | MD | | | | receptor | | open | | |
| | | | | | | inhibitor | | | | |
| 13 | NCT02675946 | Curegenix Inc | 22-Jan-16 | Advanced Solid Tumors (several) | CGX1321 | Porcupine* | | recruiting | Inhibition | Phase 1 |
| 14 | NCT00088387 | National Institute | 23-Jul-04 | Alzheimer's Disease | Lithium | GSK3b | | completed | activation | Phase 2 |
| | | of Neurological Disorders and Stroke | | | Divalproex | GSK3b? | Depakote | ' | | |
| 15 | NCT02521844 | D3 (Drug Product and Development), Biomedical Sciences Institute | 27-Jul-15 | Solid Tumors | ETC- 1922159 | Porcupine | ETC-159 | recruiting | inhibition | Phase 1 |
| 16 | NCT01606579 | Prism Pharma Co., Ltd. | 16-May-12 | Acute/Chronic Myeloid Leukemia | PRI-724 | CBP/β-catenin | | Ongoing | Inhibition | Phase 1 Phase 2 |
| 17 | NCT01214603 | Eli Lily and Company | 29-Sep-10 | Leukemia | LY2090314 | GSK3 | | completed | Activation | Phase 2 |
| 18 | NCT01302405 | Prism Pharma Co., Ltd. | 18-Feb-11 | Advanced Solid Tumors | PRI-724 | CBP/β-catenin | | terminated | inhibition | Phase 1 |
| 19 | NCT01469975 | Centre Leon Berard | 03-Nov-11 | Synovial Sarcoma | OTSA101- DTPA-90Y | Frizzled 10 neutralizing antibody | OTSA101 (unlabeled) | ongoing | Inhibition | Phase 1 |
| 20 | NCT02503137 | Samumed LLC | 16-Jul-15 | Androgenetic Alopecia | SM04554 | Not specified | | ongoing | Activation | Phase 2 |
| 21 | NCT01985763 | Randall F. Holcombe | 09-Nov-13 | CRC | Genistein | epigenetic modification of Sfrp2, Sfrp5and | | Recruiting | Inhibition | Phase 1 Phase 2 |
| 22 | NCT01457417 | Leap Therapeutics | 18-Oct-11 | Multiple Myeloma; Solid Tumors; Non-Small Cell Lung Cancer | DKN-01 | Dkk1 neutralizing antibody | | completed | activation | Phase 1 |

| Number | Identifier | Sponsor | Date Received | Condition | Intervention | target/method | Aliases | Status | Inhibition/A | Phase |
|--------|-------------|--|----------------------|---|------------------------|---|---------|------------|--------------|-----------------------|
| | | | | | | of action | | | ctivation | |
| 23 | NCT01608867 | OncoMed Pharmaceuticals, Inc. | 29-May-12 | Solid Tumors | OMP-54F28 | Wnt ligands | | Ongoing | Inhibition | Phase 1 |
| 24 | NCT01197209 | Momotaro-Gene Inc. | 03-Sep-10 | Prostate Cancer | AD- REIC/Dkk3 | LRP5/6 | Dkk3 | withdrawn | Inhibition | Phase 1 |
| 25 | NCT01931046 | Momotaro-Gene Inc. | 21-Aug-13 | Localized Prostrate Cancer | Ad5-SGE- REIC/Dkk-3 | LRP5/6 | Dkk3 | recruiting | | Phase 1 Phase 2 |
| 26 | NCT02375880 | Leap Therapeutics | 18-Feb-15 | Carcinoma of Intrahepatic and Extra-hepatic Biliary System; Carcinoma of Gallbladder; Bile Duct Cancer; Cholangiocarcinoma | DKN-01 | Dkk1 neutralizing antibody | | recruiting | activation | Phase 1 |
| 27 | NCT00741377 | Novartis Pharmaceuticals | 22-Aug-08 | Multiple Myeloma Bone Disease | BHQ880 | Dkk1 neutralizing antibody | | completed | activation | Phase 1 |
| 28 | NCT01337752 | Novartis Pharmaceuticals | 12-Apr-11 | Multiple Myeloma Renal Insufficiency | BHQ880 | Dkk1 neutralizing antibody | | completed | activation | Phase 2 |
| 29 | NCT01302886 | Novartis Pharmaceuticals | 26-Jan-11 | Smoldering Multiple Myeloma | BHQ880 | Dkk1 neutralizing antibody | | completed | activation | Phase 2 |
| 30 | NCT01882660 | Academisch Medisch Centrum Universiteit van Amsterdam (AMC- UvA) | 24-May-13 | Colon Cancer | Decitabine | Wnt target genes derepression by demethylation | | recruiting | activation | Not Applicab le |
| 31 | NCT01293487 | Pfizer | 09-Feb-11 | Osteopenia; Osteoporosis; Bone Disease | RN564 | Dkk1 neutralizing antibody | | completed | activation | Phase 1 |
| 32 | NCT02013154 | Leap Therapeutics | 11-Dec-13 | Esophageal Neoplasms; Adenocarcinoma of the Gastroesophageal Junction;. Gastroesophageal Cancer; Squamous Cell Carcinoma | DKN-01 | Dkk1 neutralizing antibody | | recruiting | activation | Phase 1 |

| Number | Identifier | Sponsor | Date Received | Condition | Intervention | target/method | Aliases | Status | Inhibition/A | Phase |
|--------|-------------|-------------------|----------------------|------------------|--------------|---------------|---------|-----------|--------------|---------|
| | | | | | | of action | | | ctivation | |
| 33 | NCT01711671 | Leap Therapeutics | 18-Oct-12 | Multiple Myeloma | DKN-01 | Dkk1 | | completed | activation | Phase 1 |
| | | | | | | neutralizing | | | | Phase 2 |
| | | | | | | antibody | | | | |
| 34 | NCT01457417 | Leap Therapeutics | 18-Oct-11 | Multiple Myeloma | DKN-01 | Dkk1 | | completed | activation | Phase 1 |
| | | | | | | neutralizing | | | | |
| | | | | | | antibody | | | | |