

[0006] Fusion constructs do not require cells to divide in order to kill the target cells. Furthermore, the fusion constructs are not likely to be immunogenic because they can be made to be relatively small in size. In addition, the fusion constructs kill multi-drug resistant cells.

[0007] Presented herein, in some [aspectsexamples](#), are methods of treating neoplastic disorders and cancers with a combination of a fusion construct and a checkpoint inhibitor.

[0008] In some [aspectsexamples](#), there is provided the use of a combination of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for reducing or inhibiting proliferation of the cell.

[0009] Data presented herein demonstrates that a fusion construct used in combination with a checkpoint inhibitor provides synergistic anti-cancer effects. In some [aspectsexamples](#), presented herein is a method of reducing or inhibiting proliferation of a cell, comprising contacting the cell with a fusion construct and a checkpoint inhibitor in an amount sufficient to reduce or inhibit proliferation of the cell, where the fusion construct comprises a first domain and a second domain, where the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety. In some [embodimentsexamples](#), a first domain of a fusion construct consists of an amino acid sequence selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue.

[0010] In some [embodimentsexamples](#), a binding moiety of a fusion construct binds to a receptor, ligand, or antigen. In certain [embodimentsexamples](#), the receptor, the ligand, or the antigen is expressed on the cell (e.g., a target cell). In certain [embodimentsexamples](#), the ligand comprises a receptor agonist or antagonist.

[0011] In certain [embodimentexamples](#), the cell is a hyperproliferating cell. In certain [embodimentexamples](#), the cell is a neoplastic, tumor, cancer or malignant cell. In certain [embodimentexamples](#), the cell is a breast, ovarian, uterine, cervical, prostate, testicular, adrenal, pituitary or endometrial cell.

[0012] In certain [embodimentexamples](#), the cell expresses a receptor, ligand, or an antigen. In certain [embodimentexamples](#), the cell expresses a hormone or a hormone receptor. In certain [embodimentexamples](#), the cell expresses a sex or gonadal steroid hormone or a sex or gonadal steroid hormone receptor.

[0013] In certain [embodimentexamples](#), the cell expresses a receptor that binds to gonadotropin-releasing hormone I, gonadotropin-releasing hormone II, lamprey III luteinizing hormone releasing hormone, luteinizing hormone beta chain, luteinizing hormone, chorionic gonadotropin, chorionic gonadotropin beta subunit, melanocyte stimulating hormone, estradiol, diethylstilbestrol, dopamine, somatostatin, follicle-stimulating hormone (FSH), glucocorticoid, estrogen, testosterone, androstenedione, dihydrotestosterone, dehydroepiandrosterone, progesterone, androgen, epidermal growth factor (EGF), growth hormone (GH), Her2/neu, vitamin H, folate, transferrin, thyroid stimulating hormone (TSH), endothelin, bombesin, growth hormone, vasoactive intestinal peptide, lactoferrin, an integrin, nerve growth factor, CD-8, CD-33, CD19, CD20, CD40, ROR1, IGF-1, carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), prostate specific antigen (PSA), prostate specific membrane antigen (PSMA), CA 125 (residual epithelial ovarian cancer), soluble Interleukin-2 (IL-2) receptor, RAGE-1, tyrosinase, MAGE-1, MAGE-2, NY-ESO-1, Melan-A/MART-1, glycoprotein (gp) 75, gp100, beta-catenin, PRAME, MUM-1, ZFP161, Ubiquitin-1, HOX-B6, YB-1, Osteonectin, ILF3, folic acid or a derivative thereof, a tumor necrosis factor (TNF) family member, TNF-alpha, TNF-beta (lymphotoxin, LT), TRAIL, Fas, LIGHT, 41BB, transforming growth factor alpha, transforming growth factor beta, insulin, ceruloplasmin, HIV-tat, a peptide or protein comprising an RGD sequence motif, a mono- saccharide, di-saccharide, oligo-saccharide, sialic acid, galactose, mannose, fucose, or acetylneuraminic acid, or an analogue thereof.

[0014] In certain [embodimentexamples](#), the cell expresses a receptor that binds to luteinizing hormone releasing hormone (LHRH). In certain [embodimentexamples](#), the integrin is selected from alpha-5 beta 3 or alpha-5 beta 1 integrin. In certain [embodimentexamples](#), the cell expresses a receptor that binds to gonadotropin-releasing hormone I, gonadotropin-releasing hormone II, lamprey III luteinizing hormone releasing hormone, luteinizing hormone beta chain, luteinizing hormone, chorionic gonadotropin, chorionic gonadotropin beta subunit, melanocyte stimulating hormone, estradiol, diethylstilbestrol, dopamine, somatostatin, follicle-stimulating hormone (FSH), glucocorticoid, estrogen, testosterone, androstenedione, dihydrotestosterone, dehydroepiandrosterone, progesterone, androgen, epidermal growth factor (EGF), growth hormone (GH), Her2/neu, vitamin H, folate, transferrin, thyroid stimulating hormone (TSH), endothelin, bombesin, vasoactive intestinal peptide, lactoferrin, an integrin, nerve growth factor, CD-8, CD-33, CD19, CD20, CD40, ROR1, IGF-1 carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), prostate specific antigen (PSA), prostate specific membrane

antigen (PSMA), CA 125 (residual epithelial ovarian cancer), soluble Interleukin-2 (IL-2) receptor, RAGE-1, tyrosinase, MAGE-1, MAGE-2, NY-ESO-1, Melan-A/MART-1, glycoprotein (gp) 75, gp100, beta-catenin, PRAME, MUM-1, ZFP161, Ubiquilin-1, HOX-B6, YB-1, Osteonectin, and ILF3.

[0015] In certain ~~embodiment~~examples, the binding moiety comprises a ligand, receptor or an antibody. In certain ~~embodiment~~examples, the binding moiety comprises a peptide, polypeptide, protein, nucleic acid or carbohydrate. In certain ~~embodiment~~examples, the binding moiety is a hormone, a hormone analogue, a fragment of a hormone or hormone analogue that binds to a hormone receptor, a hormone receptor or an agent that binds to a hormone or to a hormone receptor. In certain ~~embodiment~~examples, the binding moiety has a linear or cyclic structure.

[0016] In certain ~~embodiment~~examples, the binding moiety binds to a hormone or a hormone receptor. In certain ~~embodiment~~examples, the hormone is selected from a gonadotropin-releasing hormone I, gonadotropin-releasing hormone II, luteinizing hormone releasing hormone, lamprey III luteinizing hormone releasing hormone, luteinizing hormone beta chain, luteinizing hormone, chorionic gonadotropin, chorionic gonadotropin beta subunit, melanocyte stimulating hormone, estradiol, diethylstilbestrol, dopamine, somatostatin, follicle-stimulating hormone (FSH), glucocorticoid, estrogen, testosterone, androstenedione, dihydrotestosterone, dehydroepiandrosterone, progesterone, or an androgen. In certain ~~embodiment~~examples, the hormone analogue is selected from mifepristone, flutamide, lupron, zoladex, supprelin, synatel triptorelin, buserelin, cetorelix, ganirelix, abarelix, antide, teverelix and degarelix (Fe200486).

[0017] In certain ~~embodiment~~examples, the cell expresses a receptor, ligand or antigen, and the binding moiety of the peptide binds to the receptor, ligand, or antigen expressed by the cell. In certain ~~embodiment~~examples, the cell is a hyperproliferating cell.

[0018] In some ~~aspect~~examples, presented herein is a method of treating a subject having a hyperproliferative disorder, comprising administering to the subject a fusion construct and a checkpoint inhibitor in an amount sufficient to treat the hyperproliferative disorder, where the fusion construct comprises a first domain and a second domain, where the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety. In some

~~embodiment~~examples, the subject has a neoplasia, tumor, cancer or malignancy, and the amount sufficient to treat the hyperproliferative disorder is an amount sufficient to reduce or inhibit proliferation of the neoplasia, tumor, cancer or malignancy.

[0019] In some ~~aspect~~examples, there is provided the use of combination of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for the treatment of hyperproliferative disorder.

[0020] In some ~~aspect~~examples, presented herein is a method of reducing or inhibiting metastasis of a neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from a primary neoplasia, tumor, cancer or malignancy, comprising administering to the subject a fusion construct and a checkpoint inhibitor in an amount sufficient to reduce or inhibit metastasis of the neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from the primary neoplasia, tumor, cancer or malignancy, where the fusion construct comprises a first domain and a second domain, where the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety.

[0021] In some ~~aspect~~examples, there is provided the use of a combination of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for reducing or inhibiting metastasis of a neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from a primary neoplasia, tumor, cancer or malignancy.

[0022] In some ~~embodiment~~examples, the neoplasia, tumor, cancer or malignancy is metastatic, non-metastatic or benign. In some ~~embodiment~~examples, the neoplasia, tumor, cancer or malignancy comprises a solid cellular mass. In some ~~embodiment~~examples, the neoplasia, tumor, cancer or malignancy comprises hematopoietic cells.

[0023] In some ~~embodiment~~examples, the neoplasia, tumor, cancer or malignancy comprises a carcinoma, sarcoma, lymphoma, leukemia, adenoma, adenocarcinoma, melanoma, glioma, glioblastoma, meningioma, neuroblastoma, retinoblastoma, astrocytoma, oligodendrocytoma, mesothelioma,

reticuloendothelial, lymphatic or haematopoietic neoplasia, tumor, cancer or malignancy. In some [embodimentexamples](#), the sarcoma comprises a lymphosarcoma, liposarcoma, osteosarcoma, chondrosarcoma, leiomyosarcoma, rhabdomyosarcoma or fibrosarcoma.

[0024] In some [embodimentexamples](#), the haematopoietic neoplasia, tumor, cancer or malignancy comprises a myeloma, lymphoma or leukemia. In some [embodimentexamples](#), the neoplasia, tumor, cancer or malignancy comprises a lung, thyroid, head or neck, nasopharynx, throat, nose or sinuses, brain, spine, breast, adrenal gland, pituitary gland, thyroid, lymph, gastrointestinal (mouth, esophagus, stomach, duodenum, ileum, jejunum (small intestine), colon, rectum), genito-urinary tract (uterus, ovary, cervix, endometrial, bladder, testicle, penis, prostate), kidney, pancreas, liver, bone, bone marrow, lymph, blood, muscle, or skin neoplasia, melanoma of the eye, tumor, or cancer.

[0025] In some [embodimentexamples](#), the lung neoplasia, tumor, cancer or malignancy comprises small cell lung or non-small cell lung cancer. In some [embodimentexamples](#), the neoplasia, tumor, cancer or malignancy comprises a stem cell neoplasia, tumor, cancer or malignancy.

[0026] In some [embodimentexamples](#), the method inhibits or reduces relapse or progression of the neoplasia, tumor, cancer or malignancy.

[0027] In some [embodimentexamples](#), a method herein further comprises administering an anti-cell proliferative, anti-neoplastic, anti-tumor, anti-cancer or immune-enhancing treatment or therapy. In some [embodimentexamples](#), the treatment or therapy comprises surgical resection, radiotherapy, ionizing or chemical radiation therapy, chemotherapy, immunotherapy, local or regional thermal (hyperthermia) therapy, or vaccination. In some [embodimentexamples](#), the treatment or therapy comprises administering an alkylating agent, anti-metabolite, plant extract, plant alkaloid, nitrosourea, hormone, nucleoside or nucleotide analogue. In some [embodimentexamples](#), the treatment or therapy comprises administering cyclophosphamide, azathioprine, cyclosporin A, prednisolone, melphalan, chlorambucil, mechlorethamine, busulfan, methotrexate, 6-mercaptopurine, thioguanine, 5-fluorouracil, cytosine arabinoside, AZT, 5-azacytidine (5-AZC) and 5-azacytidine related compounds, bleomycin, actinomycin D, mithramycin, mitomycin C, carmustine, lomustine, semustine, streptozotocin, hydroxyurea, cisplatin, carboplatin, oxaliplatin, oxiplatin, mitotane, procarbazine, dacarbazine, taxol, vinblastine, vincristine, doxorubicin, dibromomannitol, irinotecan, topotecan, etoposide, teniposide, gemcitabine, or pemetrexed. In some [embodimentexamples](#), the treatment or therapy comprises administering a lymphocyte, plasma cell, macrophage, dendritic cell, NK cell or B-cell. In some [embodimentexamples](#), the treatment or therapy comprises administering an antibody, a cell growth factor, a cell survival factor, a cell differentiative factor, a cytokine or a chemokine. In some [embodimentexamples](#), the treatment or therapy comprises administering IL-2, IL-1 α , IL-1 β , IL-3, IL-6, IL-7, granulocyte-macrophage-colony stimulating factor (GM-CSF), IFN- γ , IL-12, TNF- α , TNF β , MIP-1(α , β , or γ), MIP-2, MIP-(2, 3 α , 3 β or 5), RANTES, SDF-1, MCP-1, MCP-2, MCP-3, MCP-4, eotaxin, eotaxin-2, I-309/TCA3, ATAC, HCC-1, HCC-2, HCC-3, LARC/MIP-3 α , PARC, TARC, CK β , CK β 6, CK β 7, CK β 8, CK β 9, CK β 11,

CKβ12, C10, IL-8, GRO α, GROβ, ENA-78, GCP-2, PBP/CTAPIIIβ-TG/NAP-2, Mig, PBSF/SDF-1, or lymphotactin. In some [embodimentexamples](#), a treatment or therapy comprises administering a poly ADP ribose polymerase (PARP) inhibitor, non-limiting examples of which include olaparib, rucaparib, niraparib, talazoparib, veliparib, BGB-290, CEP 9722, E7016, iniparib and 3-aminobenzamide.

[0028] In some [embodimentexamples](#), in a method described herein, a fusion construct is administered prior to, substantially contemporaneously with or following administration of an anti-cell proliferative, anti-neoplastic, anti-tumor, anti-cancer or immune-enhancing treatment or therapy. In some [embodimentexamples](#), a fusion construct is administered prior to, substantially contemporaneously with or following administration of the checkpoint inhibitor.

[0029] In some [embodimentexamples](#), of a method herein, a subject is a mammal. In some [embodimentexamples](#), a subject is a human.

[0030] In some [embodimentexamples](#), a subject has undergone surgical resection, chemotherapy, immunotherapy, ionizing or chemical radiotherapy, local or regional thermal (hyperthermia) therapy, or vaccination. In some [embodimentexamples](#), a subject is a candidate for surgical resection, chemotherapy, immunotherapy, ionizing or chemical radiotherapy, local or regional thermal (hyperthermia) therapy, or vaccination.

[0031] In some [embodimentexamples](#), a subject is not a candidate for surgical resection, chemotherapy, immunotherapy, ionizing or chemical radiotherapy, local or regional thermal (hyperthermia) therapy, or vaccination. In some [embodimentexamples](#), a treatment results in partial or complete destruction of the neoplastic, tumor, cancer or malignant cell mass, volume, size or numbers of cells, stimulating, inducing or increasing neoplastic, tumor, cancer or malignant cell necrosis, lysis or apoptosis, reducing neoplasia, tumor, cancer or malignancy volume size, cell mass, inhibiting or preventing progression or an increase in neoplasia, tumor, cancer or malignancy volume, mass, size or cell numbers, or prolonging lifespan. In some [embodimentexamples](#), a treatment results in reducing or decreasing severity, duration or frequency of an adverse symptom or complication associated with or caused by the neoplasia, tumor, cancer or malignancy. In some [embodimentexamples](#), a treatment results in reducing or decreasing pain, discomfort, nausea, weakness or lethargy. In some [embodimentexamples](#), a treatment results in increased energy, appetite, improved mobility or psychological well being.

[0032] In some [aspectexamples](#), presented herein is a method of reducing or treating benign prostate hyperplasia, comprising administering to the animal a fusion construct and a checkpoint inhibitor in an amount sufficient to treat benign prostate hyperplasia, where the fusion construct comprises a first domain and a second domain, where the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a

peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety.

[0033] In some [aspectexamples](#), there is provided the use of a combination of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for reducing or treating benign prostate hyperplasia.

[0034] In some [embodimentexamples](#), a fusion construct has greater anti-cell proliferative activity than Phor21-βCG-ala, Phor21-GSGGS-βCG-ala, Phor21-ASAAS-βCG-ala, or Phor14-βCG-ala, as ascertained by a lower IC50 value. In some [embodimentexamples](#), a fusion construct has a smaller IC50/(HA50, hemolytic activity) ratio, than Phor21-βCG-ala, Phor21-GSGGS-βCG-ala, Phor21-ASAAS-βCG-ala, or Phor14-βCG-ala. In some [embodimentexamples](#), a fusion construct has an IC50/(HA50, hemolytic activity) ratio of less than about 0.02, 0.01, or 0.005.

[0035] In some [embodimentexamples](#), a binding moiety has a linear or cyclic structure.

[0036] In some [embodimentexamples](#), a first or second domain consists of or comprises an amino acid sequence of about 1 to 10, 10 to 20, 15 to 20, 20 to 30, 30 to 40, 40 to 50, 60 to 70, 70 to 80, 80 to 90, 90 to 100 or more amino acids.

[0037] In some [embodimentexamples](#), a first domain consists of a sequence from about 15 to about 20 amino acids. In some [embodimentexamples](#), a first domain consists of a sequence with 15, 16, 17, 18, 19 or 20 amino acids.

[0038] In some [embodimentexamples](#), a second domain consists of or comprises an amino acid sequence set forth as: SYAVALSAQAALARR. In some [embodimentexamples](#), a second domain consists of or comprises an amino acid sequence set forth as: QHWSYGLRPG.

[0039] In some [embodimentexamples](#), a first domain (e.g., a lytic domain) is positioned at the NH2-terminus relative to the second domain (e.g., a domain comprising a binding moiety). In some [embodimentexamples](#), a second domain (e.g., a domain comprising a binding moiety) is positioned at the NH2-terminus relative to the first domain (e.g., a lytic domain).

[0040] In some [embodimentexamples](#), a first domain or the second domain has one or more D-amino acids. In some [embodimentexamples](#), a first domain has a D-amino acid at any K, F or A residue.

[0041] In some [embodimentexamples](#), a first domain forms an amphipathic alpha-helix. In some [embodimentexamples](#), the first and second domains are joined by a covalent bond. In some [embodimentexamples](#), the first and second domains are joined by a peptide or a non-peptide linker. In some [embodimentexamples](#), the first and second domains are joined by peptide sequence having from 1 to 25 amino acid residues, or a linear carbon chain. In some [embodimentexamples](#), the first and second domains are joined by peptide

sequence comprising one or more A, S or G amino acid residues. In some embodimentexamples, the first and second domains are joined by peptide sequence comprising or consisting of: GSGGS (SEQ. ID NO. 10), ASAAS (SEQ. ID NO.11), or CCCCCC. In some embodimentexamples, a fusion construct comprises a third, fourth, fifth, sixth or seventh domain. In some embodimentexamples, a fusion construct is isolated or purified. In some embodimentexamples, a fusion construct comprises a mixture.

[0042] In some aspectexamples, presented herein is a method of reducing or inhibiting proliferation of a cell, comprising contacting the cell with a fusion construct and a checkpoint inhibitor in an amount sufficient to reduce or inhibit proliferation of the cell, where the fusion construct comprises a first lytic domain and a second domain, where the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1) or peptide KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog.

[0043] In some aspectexamples, presented herein is a method of treating a subject having a hyperproliferative disorder, comprising administering to the subject a fusion construct and a checkpoint inhibitor in an amount sufficient to treat the hyperproliferative disorder, where the fusion construct comprises a first lytic domain and a second domain, where the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog.

[0044] In some aspectexamples, presented herein is a method of reducing or inhibiting metastasis of a neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from a primary neoplasia, tumor, cancer or malignancy, comprising administering to the subject a fusion construct and a checkpoint inhibitor in an amount sufficient to reduce or inhibit metastasis of the neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from the primary neoplasia, tumor, cancer or malignancy, where the fusion construct comprises a first lytic domain and a second domain, where the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog.

[0045] In some aspectexamples, presented herein is a method of reducing or treating benign prostate hyperplasia, comprising administering to the animal a fusion construct and a checkpoint inhibitor in an amount sufficient to treat benign prostate hyperplasia, where the fusion construct comprises a first lytic domain and a second domain, where the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ.

ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog.

[0046] In some [embodimentexamples](#), a second domain of a fusion construct consists of, or comprises, the amino acid sequence set forth as: QHWSYGLRPG (SEQ. ID NO.9).

[0047] In some [embodimentexamples](#), the fusion construct is isolated or purified. In some [embodimentexamples](#), the fusion construct has greater anti-cell proliferative activity than Phor21-βCG-ala, Phor21-(SEQ. ID NO.10)-βCG-ala, Phor21-(SEQ. ID NO.11)-βCG-ala, or Phor14-βCG-ala, as ascertained by a lower IC50 value. In some [embodimentexamples](#), the fusion construct has a smaller IC50/HA50 (hemolytic activity) ratio, than Phor21-βCG-ala, Phor21-(SEQ. ID NO. 10)-βCG-ala, Phor21-(SEQ. ID NO.11)-βCG-ala, or Phor14-βCG-ala. In some [embodimentexamples](#), the fusion construct has an IC50/ HA50 (hemolytic activity) ratio of less than about 0.02, 0.01, or 0.005. In some [embodimentexamples](#), the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1). In some [embodimentexamples](#), the first lytic domain consists of peptide KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4).

[0048] In some [embodimentexamples](#), the LHRH analog comprises Lupron (leuprolide). In some [embodimentexamples](#), the LHRH analog comprises zoladex (goserelin). In some [embodimentexamples](#), the LHRH analog comprises supprelin (histrelin). In some [embodimentexamples](#), the LHRH analog comprises triptorelin. In some [embodimentexamples](#), the LHRH analog comprises buserelin. In some [embodimentexamples](#), the LHRH analog comprises cetorelix. In some [embodimentexamples](#), the LHRH analog comprises ganirelix. In some [embodimentexamples](#), the LHRH analog comprises abarelix. In some [embodimentexamples](#), the LHRH analog comprises antide. In some [embodimentexamples](#), the LHRH analog comprises teverelix. In some [embodimentexamples](#), the LHRH analog comprises degarelix (Fe200486). In some [embodimentexamples](#), the non-peptide linker comprises a linear carbon chain linker. In some [embodimentexamples](#), the non-peptide linker comprises a linear 6 carbon chain linker.

[0049] In some [embodimentexamples](#), a composition or a mixture comprises a fusion construct and a checkpoint inhibitor.

[0050] In some [embodimentexamples](#), a hyperproliferation disorder or cancer is an ovarian cancer or breast cancer.

[0051] In some [embodimentexamples](#), a checkpoint inhibitor is an inhibitor or antagonist of programmed death ligand 1 (PD-L1, also known as B7-H1 or CD274), programmed cell death protein 1 (PD-1) or cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). In some [embodimentexamples](#), a checkpoint inhibitor is an inhibitor of GITR (glucocorticoid-induced TNFR-related protein), VISTA (V-domain immunoglobulin (Ig)-containing suppressor of T-cell activation), TIGIT (T cell immunoreceptor with Ig and ITIM domains), LAG-3 (Lymphocyte-activation gene 3), TIM3 (T cell immunoglobulin and mucin domain-containing protein 3), IDO (Indolamine 2,3 dioxigenase), OX-40 (CD134/OX40 receptor), or anti-NKG2A (e.g., monalizumab). In some [embodimentexamples](#), a checkpoint inhibitor is a small

compound inhibitor. In some embodimentexamples, a checkpoint inhibitor is an antibody (e.g., a monoclonal antibody).

[0052] In some embodimentexamples, a checkpoint inhibitor is an antagonist antibody that binds to PD-L1 or PD-1. In some embodimentexamples, a checkpoint inhibitor is an anti-PD-L1 mouse monoclonal antibody (e.g., clone 10F.9G2). In some embodimentexamples, a checkpoint inhibitor is selected from the group consisting of ipilimumab, atezolizumab, avelumab, durvalumab, cemiplimab, nivolumab and pembrolizumab.

[0053] Subjects treatable in accordance with the methods include mammals. In particular embodimentexamples, a subject is a human.

[0053a] In one aspect, presented herein is a method of reducing or inhibiting proliferation of a cell, comprising contacting the cell with a fusion construct and a checkpoint inhibitor in an amount sufficient to reduce or inhibit proliferation of the cell, wherein the fusion construct comprises a first domain and a second domain, wherein the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety.

[0053b] In another aspect, presented herein is a use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for treating a hyperproliferative disorder, wherein the fusion construct comprises a first domain and a second domain, wherein the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of

the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety, wherein the medicament is to be administered to a subject.

[0053c] In another aspect, presented herein is a use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for reducing or inhibiting metastasis of a neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from a primary neoplasia, tumor, cancer or malignancy, wherein the fusion construct comprises a first domain and a second domain, wherein the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety, wherein the medicament is to be administered to a subject.

[0053d] In another aspect, presented herein is a use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for treating benign prostate hyperplasia, wherein the fusion construct comprises a first domain and a second domain, wherein the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety, wherein the medicament is to be administered to an animal.

[0053e] In another aspect, presented herein is method of reducing or inhibiting proliferation of a cell, comprising contacting the cell with a fusion construct and a checkpoint inhibitor in an amount sufficient to reduce or inhibit proliferation of the cell,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog.

[0053f] In another aspect, presented herein is a use of a fusion construct and a checkpoint in the manufacture of a medicament for treating a hyperproliferative disorder,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog, wherein the medicament is to be administered to a subject.

[0053g] In another aspect, presented herein is a use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for reducing or inhibiting metastasis of a neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from the primary neoplasia, tumor, cancer or malignancy,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog, wherein the medicament is to be administered to a subject.

[0053h] In another aspect, presented herein is a use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for treating benign prostate hyperplasia,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog, wherein the medicament is to be administered to an animal.

[0053i] In another aspect, presented herein is a use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for treating an ovarian cancer or breast cancer,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog, wherein the checkpoint inhibitor comprises an inhibitor an antagonist of PD-L1, PD-1 or CTLA-4, and wherein the cancer is selected from ovarian cancer, breast cancer, melanoma and hepatocellular carcinoma, and wherein the medicament is to be administered to a subject-.

Description of Drawings

[0054] **Figure 1** shows that LHRH-Phor21 kills cancer cells faster than Phor21-βCG-ala. Human melanoma cells (MDA-MB-435S.luc, various passage numbers) were incubated with Phor21-βCG-ala or LHRH-Phor21.

[0055] **Figure 2** shows cytotoxicity to MDA-MB-435S.luc cell (micromolar IC₅₀) of βCG-ala fusion constructs having 21 (Phor21), 18 (Phor18 (338983) = CLIP71) and 15 (Phor15) amino acids in their lytic domain, compared to Phor21-βCG-ala.

[0056] **Figure 3** shows cytotoxicity to MDA-MB-435S.luc cells (micromolar IC₅₀) of βCG-ala and LHRH fusion constructs. Fusion constructs more toxic to MDA-MB-435S.luc cells than Phor21-βCG-ala are listed to the right of the figure.

[0057] **Figure 4** shows cytotoxicity to MDA-MB-435S.luc cell (micromolar IC₅₀) of luteinizing hormone-releasing hormone (LHRH) fusion constructs. The fusion constructs are: 323033 = Phor21-βCG-ala, 337479 = LHRH-Phor21, 337480 = Phor21-LHRH, 338611 = D-ala-Phor21-LHRH, 338612 = Phor18-ASAAS-LHRH, 338613 = Phor18-LHRH (EP-100), 339385 = D-ala-Phor18-LHRH, and 339347 = Phor18-Lupron.

[0058] **Figure 5** shows acute hemolytic activity (micromolar HA₅₀) of βCG-ala and LHRH fusion constructs to human red blood cells compared to Phor21-βCG-ala. All fusion constructs had significantly lower hemolytic activity than Phor21-βCG-ala, except for LHRH-Phor21, Phor21-LHRH and Phor18-Lupron (QHWSY(D-Leu)LRPNEt = Lupron).

[0059] **Figure 6** shows a comparison of cytotoxicity and hemolytic activity. Peptides indicated with arrows are more toxic to cells than Phor21-βCG-ala.

[0060] **Figure 7** is a treatment schedule outline.

[0061] **Figures 8A-8J** is a summary of tumor conditions during treatment and at study endpoint with 3 βCG conjugates in comparison to unconjugated Phor21, unconjugated Phor18 (338983)=(CLIP71) and an (KKKFAFA)₃ conjugate (338984). Fusion construct codes, 33 = Phor21β-CG-ala; 76 = Phor18-βCG-ala; 81 = D-ala-Phor21-βCG-ala; 85 = D-ala-Phor18-LHRH; 47 = Phor18-Lupron; 13 = Phor18-

What is Claimed:

1. A method of reducing or inhibiting proliferation of a cell, comprising contacting the cell with a fusion construct and a checkpoint inhibitor in an amount sufficient to reduce or inhibit proliferation of the cell, wherein the fusion construct comprises a first domain and a second domain, wherein the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety.

2. The method of claim 1, wherein the first domain consists of an amino acid sequence selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); or an amino acid sequence selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue.

3. The method of claims 1 or 2, wherein the binding moiety binds to a receptor, ligand, or antigen.

4. The method of claim 3, wherein the receptor, the ligand, or the antigen is expressed on the cell.

5. The method of claim 3 or 4, wherein the ligand comprises a receptor agonist or antagonist.

6. The method of any of one of claims 1 to 5, wherein the cell is a hyperproliferating cell.

7. The method of claim 6, wherein the cell is a neoplastic, tumor, cancer or malignant cell.

8. The method of claim 6, wherein the cell is a breast, ovarian, uterine, cervical, prostate, testicular, adrenal, pituitary or endometrial cell.

9. The method of any one of claims 1 to 8, wherein the cell expresses a receptor, ligand, or an antigen.

10. The method of any one of claims 1 to 9, wherein the cell expresses a hormone or a hormone receptor.

11. The method of any one of claims 1 to 10, wherein the cell expresses a sex or gonadal steroid hormone or a sex or gonadal steroid hormone receptor.

12. The method of any one of claims 1 to 11, wherein the cell expresses a receptor that binds to gonadotropin-releasing hormone I, gonadotropin-releasing hormone II, lamprey III luteinizing hormone releasing hormone, luteinizing hormone beta chain, luteinizing hormone, chorionic gonadotropin, chorionic gonadotropin beta subunit, melanocyte stimulating hormone, estradiol, diethylstilbestrol, dopamine, somatostatin, follicle-stimulating hormone (FSH), glucocorticoid, estrogen, testosterone, androstenedione, dihydrotestosterone, dehydroepiandrosterone, progesterone, androgen, epidermal growth factor (EGF), growth hormone (GH), Her2/neu, vitamin H, folate, transferrin, thyroid stimulating hormone (TSH), endothelin, bombesin, growth hormone, vasoactive intestinal peptide, lactoferrin, an integrin, nerve growth factor, CD-8, CD-33, CD19, CD20, CD40, ROR1, IGF-1, carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), prostate specific antigen (PSA), prostate specific membrane antigen (PSMA), CA 125 (residual epithelial ovarian cancer), soluble Interleukin-2 (IL-2) receptor, RAGE-1, tyrosinase, MAGE-1, MAGE-2, NY-ESO-1, Melan-A/MART-1, glycoprotein (gp) 75, gp100, beta-catenin, PRAME, MUM-1, ZFP161, Ubiquitin-1, HOX-B6, YB-1, Osteonectin, ILF3, folic acid or a derivative thereof, a tumor necrosis factor (TNF) family member, TNF-alpha, TNF-beta (lymphotoxin, LT), TRAIL, Fas, LIGHT, 41BB, transforming growth factor alpha, transforming growth factor beta, insulin, ceruloplasmin, HIV-tat, a peptide or protein comprising an RGD sequence motif, a mono- saccharide, di- saccharide, oligo-saccharide, sialic acid, galactose, mannose, fucose, or acetylneuraminic acid, or an analogue thereof.

13. The method of any one of claims 1 to 12, wherein the cell expresses a receptor that binds to luteinizing hormone releasing hormone (LHRH).

14. The method of claim 12, wherein the integrin is selected from alpha-5 beta 3 or alpha-5 beta 1 integrin.

15. The method of any one of claims 1 to 14, wherein the cell expresses a receptor that binds to gonadotropin-releasing hormone I, gonadotropin-releasing hormone II, lamprey III luteinizing hormone releasing hormone, luteinizing hormone beta chain, luteinizing hormone, chorionic gonadotropin, chorionic gonadotropin beta subunit, melanocyte stimulating hormone, estradiol, diethylstilbestrol, dopamine, somatostatin, follicle-stimulating hormone (FSH), glucocorticoid, estrogen, testosterone, androstenedione, dihydrotestosterone, dehydroepiandrosterone, progesterone, androgen, epidermal growth factor (EGF), growth hormone (GH), Her2/neu, vitamin H, folate, transferrin, thyroid

stimulating hormone (TSH), endothelin, bombesin, vasoactive intestinal peptide, lactoferrin, an integrin, nerve growth factor, CD-8, CD-33, CD19, CD20, CD40, ROR1, IGF-1 carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), prostate specific antigen (PSA), prostate specific membrane antigen (PSMA), CA 125 (residual epithelial ovarian cancer), soluble Interleukin-2 (IL-2) receptor, RAGE-1, tyrosinase, MAGE-1, MAGE-2, NY-ESO-1, Melan-A/MART-1, glycoprotein (gp) 75, gp100, beta-catenin, PRAME, MUM-1, ZFP161, Ubiquilin-1, HOX-B6, YB-1, Osteonectin, or ILF3.

16. The method of any one of claim 1 to 15, wherein the binding moiety comprises a ligand, receptor or an antibody.

17. The method of any one of claims 1 to 16, wherein the binding moiety comprises a peptide, polypeptide, protein, nucleic acid or carbohydrate.

18. The method of any one of claims 1 to 17, wherein the binding moiety is a hormone, a hormone analogue, a hormone analogue that binds to a hormone receptor, a fragment of a hormone, a hormone receptor, or an agent that binds to a hormone or to a hormone receptor.

19. The method of any one of claims 1 to 18, wherein the binding moiety has a linear or cyclic structure.

20. The method of any one of claims 1 to 19, wherein the binding moiety binds to a hormone or a hormone receptor.

21. The method of claim 20, wherein the hormone is selected from a gonadotropin-releasing hormone I, gonadotropin-releasing hormone II, luteinizing hormone releasing hormone, lamprey III luteinizing hormone releasing hormone, luteinizing hormone beta chain, luteinizing hormone, chorionic gonadotropin, chorionic gonadotropin beta subunit, melanocyte stimulating hormone, estradiol, diethylstilbestrol, dopamine, somatostatin, follicle-stimulating hormone (FSH), glucocorticoid, estrogen, testosterone, androstenedione, dihydrotestosterone, dehydroepiandrosterone, progesterone, or an androgen.

22. The method of claim 18, wherein the hormone analogue is selected from mifepristone, flutamide, lupron, zoladex, supprelin, synatel triptorelin, buserelin, cetorelix, ganirelix, abarelix, antide, teverelix and degarelix (Fe200486).

23. The method of any one of claims 1 to 22, wherein the cell expresses a receptor, ligand or antigen, and the binding moiety of the peptide binds to the receptor, ligand, or antigen expressed by the cell.

24. The method of claim 23, wherein the cell is a hyperproliferating cell.

25. ~~A method of treating a subject having a hyperproliferative disorder, comprising administering to the subject~~ Use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for treating ~~in an amount sufficient to treat the a~~ hyperproliferative disorder,

wherein the fusion construct comprises a first domain and a second domain, wherein the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety.

wherein the medicament is to be administered to a subject.

26. The ~~method-use~~ of claim 25, wherein the subject has a neoplasia, tumor, cancer or malignancy, and the medicament is to be administered in an amount sufficient to treat the hyperproliferative disorder is an amount sufficient to reduce or inhibit proliferation of the neoplasia, tumor, cancer or malignancy.

27. ~~A method of reducing or inhibiting metastasis of a neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from a primary neoplasia, tumor, cancer or malignancy, comprising administering to the subject~~ Use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for reducing or inhibiting an amount sufficient to reduce or inhibit metastasis of ~~the a~~ neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from ~~the a~~ primary neoplasia, tumor, cancer or malignancy,

wherein the fusion construct comprises a first domain and a second domain, wherein the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue,

or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety.

wherein the medicament is to be administered to a subject.

28. The ~~method~~use of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy is metastatic, non-metastatic or benign.

29. The ~~method~~use of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy comprises a solid cellular mass.

30. The ~~method~~use of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy comprises hematopoietic cells.

31. The ~~method~~use of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy comprises a carcinoma, sarcoma, lymphoma, leukemia, adenoma, adenocarcinoma, melanoma, glioma, glioblastoma, meningioma, neuroblastoma, retinoblastoma, astrocytoma, oligodendrocytoma, mesothelioma, reticuloendothelial, lymphatic or haematopoietic neoplasia, tumor, cancer or malignancy.

32. The ~~method~~use of claim 31, wherein the sarcoma comprises a lymphosarcoma, liposarcoma, osteosarcoma, chondrosarcoma, leiomyosarcoma, rhabdomyosarcoma or fibrosarcoma.

33. The ~~method~~use of claim 31, wherein the haematopoietic neoplasia, tumor, cancer or malignancy comprises a myeloma, lymphoma or leukemia.

34. The ~~method~~use of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy comprises a lung, thyroid, head or neck, nasopharynx, throat, nose or sinuses, brain, spine, breast, adrenal gland, pituitary gland, thyroid, lymph, gastrointestinal (mouth, esophagus, stomach, duodenum, ileum, jejunum (small intestine), colon, rectum), genito-urinary tract (uterus, ovary, cervix, endometrial, bladder, testicle, penis, prostate), kidney, pancreas, liver, bone, bone marrow, lymph, blood, muscle, or skin neoplasia, ocular melanoma, tumor, or cancer.

35. The ~~method~~use of claim 34, wherein the lung neoplasia, tumor, cancer or malignancy comprises ovarian cancer or melanoma.

36. The ~~method~~use of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy comprises a stem cell neoplasia, tumor, cancer or malignancy.

37. The ~~method~~use of claim 26 or 27, wherein the ~~method~~use inhibits or reduces relapse or progression of the neoplasia, tumor, cancer or malignancy.

38. The ~~method~~use of claim 26 or 27, further comprising ~~administering~~ an anti-cell proliferative, anti-neoplastic, anti-tumor, anti-cancer or immune-enhancing treatment or therapy which is to be administered to the subject.

39. The ~~method~~use of claim 38, wherein the treatment or therapy comprises surgical resection, radiotherapy, ionizing or chemical radiation therapy, chemotherapy, immunotherapy, local or regional thermal (hyperthermia) therapy, or vaccination.

40. The ~~method~~use of claim 38, wherein the treatment or therapy comprises ~~administering~~ an alkylating agent, anti-metabolite, plant extract, plant alkaloid, nitrosourea, hormone, nucleoside or nucleotide analogue which is to be administered to the subject.

41. The ~~method~~use of claim 38, wherein the treatment or therapy comprises ~~administering a~~ cyclophosphamide, azathioprine, cyclosporin A, prednisolone, melphalan, chlorambucil, mechlorethamine, busulfan, methotrexate, 6-mercaptopurine, thioguanine, 5-fluorouracil, cytosine arabinoside, AZT, 5-azacytidine (5-AZC) and 5-azacytidine related compounds, bleomycin, actinomycin D, mithramycin, mitomycin C, carmustine, lomustine, semustine, streptozotocin, hydroxyurea, cisplatin, mitotane, procarbazine, dacarbazine, taxol, vinblastine, vincristine, doxorubicin, dibromomannitol or a PARP inhibitor which is to be administered to the subject.

42. The ~~method~~use of claim 38, wherein the treatment or therapy comprises ~~administering a~~ lymphocyte, plasma cell, macrophage, dendritic cell, NK cell or B-cell which is to be administered to the subject.

43. The ~~method~~use of claim 38, wherein the treatment or therapy comprises ~~administering an~~ antibody, a cell growth factor, a cell survival factor, a cell differentiative factor, a cytokine or a chemokine which is to be administered to the subject.

44. The ~~method~~use of claim 38, wherein the treatment or therapy comprises ~~administering an~~ IL-2, IL-1 α , IL-1 β , IL-3, IL-6, IL-7, granulocyte-macrophage-colony stimulating factor (GM-CSF), IFN- γ , IL-12, TNF- α , TNF β , MIP-1 α , MIP-1 β , RANTES, SDF-1, MCP-1, MCP-2, MCP-3, MCP-4, eotaxin, eotaxin-2, I-309/TCA3, ATAC, HCC-1, HCC-2, HCC-3, LARC/MIP-3 α , PARC, TARC, CK β , CK β 6, CK β 7, CK β 8, CK β 9, CK β 11, CK β 12, C10, IL-8, GRO α , GRO β , ENA-78, GCP-2, PBP/CTAPIII β -TG/NAP-2, Mig, PBSF/SDF-1, or lymphotactin which is to be administered to the subject.

45. The ~~method~~use of claim 38, wherein the fusion construct is to be administered prior to, substantially contemporaneously with or following administration of the anti-cell proliferative, anti-neoplastic, anti-tumor, anti-cancer or immune-enhancing treatment or therapy.

46. The ~~method~~use of any one of claims 25 to 45, wherein the subject has undergone surgical resection, chemotherapy, immunotherapy, ionizing or chemical radiotherapy, local or regional thermal (hyperthermia) therapy, or vaccination.

47. The ~~method~~use of any one of claims 25 or 45, wherein the subject is a candidate for surgical resection, chemotherapy, immunotherapy, ionizing or chemical radiotherapy, local or regional thermal (hyperthermia) therapy, or vaccination.

48. The ~~method~~use of any one of claims 25 to 45, wherein the subject is not a candidate for surgical resection, chemotherapy, immunotherapy, ionizing or chemical radiotherapy, local or regional thermal (hyperthermia) therapy, or vaccination.

49. The ~~method~~use of any one of claims 25 to 45, wherein the treatment results in partial or complete destruction of the neoplastic, tumor, cancer or malignant cell mass, volume, size or numbers of cells, stimulating, inducing or increasing neoplastic, tumor, cancer or malignant cell necrosis, lysis or apoptosis, reducing neoplasia, tumor, cancer or malignancy volume size, cell mass, inhibiting or preventing progression or an increase in neoplasia, tumor, cancer or malignancy volume, mass, size or cell numbers, or prolonging lifespan.

50. The ~~method~~use of any one of claims 25 to 45, wherein the treatment results in reducing or decreasing severity, duration or frequency of an adverse symptom or complication associated with or caused by the neoplasia, tumor, cancer or malignancy.

51. The ~~method~~use of any one of claims 25 to 45, wherein the treatment results in reducing or decreasing pain, discomfort, nausea, weakness or lethargy.

52. The ~~method~~use of any one of claims 25 to 45, wherein the treatment results in increased energy, appetite, improved mobility or psychological well being.

53. The ~~method~~use of any one of claims 25 to 45, wherein the subject is a mammal.

54. The ~~method~~use of any one of claims 25 to 45, wherein the subject is a human.

55. ~~A method of reducing or treating benign prostate hyperplasia, comprising administering to the animal~~ Use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for an amount sufficient to treat ~~treating~~ benign prostate hyperplasia,

wherein the fusion construct comprises a first domain and a second domain, wherein the first domain consists of a 12 to 28 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6), or a 12 to 25 amino acid sequence that includes a peptide selected from KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKF (SEQ. ID NO.2), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) and KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6) having one or more of the K residues substituted with any of an F or L residue, one or more of the F residues substituted with any of a K, A or L residue, or one or more of the A residues substituted with any of a K, F or L residue; and the second domain comprises a binding moiety.

wherein the medicament is to be administered to an animal.

56. The ~~method~~method of any one of claims 1 to 24 or the use of any one of claims ~~1-25~~ to 55, wherein the fusion construct has greater anti-cell proliferative activity than Phor21- β CG-ala, Phor21-GSGGS- β CG-ala, Phor21-ASAAS- β CG-ala, or Phor14- β CG-ala, as ascertained by a lower IC50 value.

57. The ~~method of any one of claims 1 to 24 or claim 56, or the use of any one of claims 25 to 55~~method of any one of claims 1 to 56, wherein the fusion construct has a smaller IC50/(HA50, hemolytic activity) ratio, than Phor21-βCG-ala, Phor21-GSGGS-βCG-ala, Phor21-ASAAS-βCG-ala, or Phor14-βCG-ala.

58. The ~~method of any one of claims 1 to 24 or claims 56 to 57, or the use of any one of claims 25 to 55~~method of any one of claims 1 to 57, wherein the fusion construct has an IC50/(HA50, hemolytic activity) ratio of less than about 0.02, 0.01, or 0.005.

59. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 58, or the use of any one of claims ~~425~~ to ~~5855~~, wherein the binding moiety has a linear or cyclic structure.

60. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 59, or the use of any one of claims ~~425~~ to ~~5955~~, wherein the first or second domain consists of or comprises an amino acid sequence of about 1 to 10, 10 to 20, 15 to 20, 20 to 30, 30 to 40, 40 to 50, 60 to 70, 70 to 80, 80 to 90, 90 to 100 or more amino acids.

61. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 60, or the use of any one of claims ~~425~~ to ~~6055~~, wherein the first domain consists of a sequence from about 15 to about 20 amino acids.

62. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 61, or the use of any one of claims ~~425~~ to ~~6455~~, wherein the first domain consists of a sequence with 15, 16, 17, 18, 19 or 20 amino acids.

63. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 62, or the use of any one of claims ~~425~~ to ~~6255~~, wherein the second domain consists of or comprises an amino acid sequence set forth as: SYAVALSAQAALARR.

64. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 63, or the use of any one of claims ~~425~~ to ~~6355~~, wherein the second domain consists of or comprises an amino acid sequence set forth as: QHWSYGLRPG.

65. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 64, or the use of any one of claims ~~425~~ to ~~6455~~, wherein the first domain is positioned at the NH₂-terminus relative to the second domain.

66. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 65, or the use of any one of claims ~~425~~ to ~~6555~~, wherein the second domain is positioned at the NH₂-terminus relative to the first domain.

67. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 66, or the use of any one of claims ~~425~~ to ~~6655~~, wherein the first domain or the second domain has one or more D-amino acids.

68. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 67, or the use of any one of claims ~~425~~ to ~~6755~~, wherein the first domain has a D-amino acid at any K, F or A residue.

69. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 68, or the use of any one of claims ~~425~~ to ~~6855~~, wherein the first domain forms an amphipathic alpha-helix.

70. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 69, or the use of any one of claims ~~425~~ to ~~6955~~, wherein the first and second domains are joined by a covalent bond.

71. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 70, or the use of any one of claims ~~425~~ to ~~7055~~, wherein the first and second domains are joined by a peptide or a non-peptide linker.

72. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 71, or the use of any one of claims ~~425~~ to ~~7155~~, wherein the first and second domains are joined by peptide sequence having from 1 to 25 amino acid residues, or a linear carbon chain.

73. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 72, or the use of any one of claims ~~425~~ to ~~7255~~, wherein the first and second domains are joined by peptide sequence comprising one or more A, S or G amino acid residues.

74. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 73, or the use of any one of claims ~~425~~ to ~~7355~~, wherein the first and second domains are joined by peptide sequence comprising or consisting of: GSGGS, ASAAS, or CCCCCC.

75. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 74, or the use of any one of claims ~~425~~ to ~~7455~~, further comprising a third, fourth, fifth, sixth or seventh domain.

76. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 75, or the use of any one of claims ~~425~~ to ~~7555~~, wherein the fusion construct is isolated or purified.

77. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 76, or the use of any one of claims ~~425~~ to ~~7655~~, wherein the fusion construct comprises a mixture.

78. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 77, or the use of any one of claims ~~425~~ to ~~7755~~, wherein the checkpoint inhibitor is an inhibitor or antagonist of programmed death ligand 1 (PD-L1), programmed cell death 1 (PD-1) or CTLA-4.

79. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 78, or the use any one of claims ~~425~~ to ~~7855~~, wherein the checkpoint inhibitor is an antagonist antibody that binds to PD-L1, PD-1 or CTLA-4.

80. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 79, or the use of any one of claims ~~425~~ to ~~7955~~, wherein the checkpoint inhibitor is selected from the group consisting of ipilimumab, atezolizumab, avelumab, durvalumab, cemiplimab, nivolumab and pembrolizumab.

81. The ~~method~~method of any one of claims 1 to 24 or claims 56 to 80, or the use of any one of claims ~~425~~ to ~~8055~~, wherein the fusion construct is to be administered prior to, substantially contemporaneously with or following administration of the checkpoint inhibitor.

82. A method of reducing or inhibiting proliferation of a cell, comprising contacting the cell with a fusion construct and a checkpoint inhibitor in an amount sufficient to reduce or inhibit proliferation of the cell,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog.

83. ~~A method of treating a subject having a hyperproliferative disorder, comprising administering to the subject~~Use of a fusion construct and a checkpoint ~~in the manufacture of a medicament for treating a~~ inhibitor in an amount sufficient to treat the hyperproliferative disorder,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog.

wherein the medicament is to be administered to a subject.

84. ~~A method of reducing or inhibiting metastasis of a neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from a primary neoplasia, tumor, cancer or malignancy, comprising administering to the subject~~Use of a fusion construct and a checkpoint inhibitor ~~in the manufacture of a medicament for reducing or inhibiting in an amount sufficient to reduce or inhibit~~ metastasis of ~~the a~~ neoplasia, tumor, cancer or malignancy to other sites, or formation or establishment of metastatic neoplasia, tumor, cancer or malignancy at other sites distal from the primary neoplasia, tumor, cancer or malignancy,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog.

wherein the medicament is to be administered to a subject.

85. ~~A method of reducing or treating benign prostate hyperplasia, comprising administering to the animal~~ Use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for treating in an amount sufficient to treat benign prostate hyperplasia,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog,

wherein the medicament is to be administered to an animal.

86. The ~~method~~ method of claim 82 or the use of any one of claims ~~82-83~~ to 85, wherein the second domain consists of or comprises the amino acid sequence set forth as: QHWSYGLRPG (SEQ. ID NO.9).

87. The ~~method of claim 82 or claim 86, or the use~~ ~~method~~ of any one of claims ~~82-83~~ to ~~86~~~~85~~, wherein the first lytic domain is positioned at the NH₂-terminus relative to the second domain.

88. The ~~method~~ method of claim 82 or claim 86, or the use of any one of claims ~~82~~~~83~~ to ~~86~~~~85~~, wherein the second domain is positioned at the NH₂-terminus relative to the first lytic domain.

89. The ~~method~~ method of claim 82 or claims 86 to 88, or the use of any one of claims ~~82~~~~83~~ to ~~88~~~~85~~, wherein the first lytic domain or the second domain has one or more D-amino acids.

90. The ~~method~~ method of claim 82 or claims 86 to 88, or the use of any one of claims ~~82~~~~83~~ to ~~88~~~~85~~, wherein the first lytic domain has a D-amino acid at any K, F or A residue.

91. The ~~method~~ method of claim 82 or claims 86 to 90, or the use of any one of claims ~~82~~~~83~~ to ~~90~~~~85~~, wherein the first lytic domain forms an amphipathic alpha-helix.

92. The ~~method~~ method of claim 82 or claims 86 to 91, or the use of any one of claims ~~82~~~~83~~ to ~~91~~~~85~~, wherein the first lytic and second domains are joined by a covalent bond.

93. The ~~method~~ method of claim 82 or claims 86 to 92, or the use of any one of claims ~~82~~~~83~~ to ~~92~~~~85~~, wherein the first lytic and second domains are joined by a peptide or a non-peptide linker.

94. The ~~method~~ method of claim 82 or claims 86 to 93, or the use of any one of claims ~~82~~~~83~~ to ~~93~~~~85~~, wherein the peptide linker has a length from 1 to 25 amino acid residues.

95. The ~~method~~ method of claim 82 or claims 86 to 94, or the use of any one of claims ~~82~~~~83~~ to ~~94~~~~85~~, wherein the first lytic and second domains are joined by peptide linker comprising one or more A, S or G amino acid residues.

96. The ~~method~~ method of claim 82 or claims 86 to 95, or the use of any one of claims ~~82~~~~83~~ to ~~95~~~~85~~, wherein the first lytic and second domains are joined by peptide linker comprising or consisting of: GSGGS (SEQ. ID NO. 10), or ASAAS (SEQ. ID NO.11).

97. The ~~method~~method of claim 82 or claims 86 to 96, or the use of any one of claims ~~8283~~8283 to ~~9685~~9685, wherein the fusion construct is isolated or purified.

98. The ~~method~~method of claim 82 or claims 86 to 97, or the use of any one of claims ~~8283~~8283 to ~~9785~~9785, wherein the fusion construct has greater anti-cell proliferative activity than Phor21-βCG-ala, Phor21-(SEQ. ID NO.10)-βCG-ala, Phor21-(SEQ. ID NO.11)-βCG-ala, or Phor14-βCG-ala, as ascertained by a lower IC₅₀ value.

99. The ~~method~~method of claim 82 or claims 86 to 98, or the use of any one of claims ~~8283~~8283 to ~~9885~~9885, wherein the fusion construct has a smaller IC₅₀/HA₅₀ (hemolytic activity) ratio, than Phor21-βCG-ala, Phor21-(SEQ. ID NO. 10)-βCG-ala, Phor21-(SEQ. ID NO.11)-βCG-ala, or Phor14-βCG-ala.

100. The ~~method~~method of claim 82 or claims 86 to 99, or the use of any one of claims ~~8283~~8283 to ~~9985~~9985, wherein the fusion construct has an IC₅₀/ HA₅₀ (hemolytic activity) ratio of less than about 0.02, 0.01, or 0.005.

101. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~10085~~10085, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1).

102. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4).

103. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the LHRH analog comprises Lupron (leuprolide).

104. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the LHRH analog comprises zoladex (goserelin).

105. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the LHRH analog comprises supprelin (histrelin).

106. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the LHRH analog comprises triptorelin.

107. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the LHRH analog comprises buserelin.

108. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the LHRH analog comprises cetorelix.

109. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the LHRH analog comprises ganirelix.

110. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the LHRH analog comprises abarelix.

111. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~8283 to ~~85400~~85400, wherein the LHRH analog comprises antide.

112. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~ to ~~85400~~, wherein the LHRH analog comprises teverelix.

113. The ~~method~~method of claim 82 or claims 86 to 100, or the use of any one of claims ~~8283~~ to ~~85400~~, wherein the LHRH analog comprises degarelix (Fe200486).

114. The ~~method~~method of claim 82 or claims 86 to 113, or the use of any one of claims ~~8283~~ to ~~85443~~, wherein the non-peptide linker comprises a linear carbon chain linker.

115. The ~~method~~method of claim 82 or claims 86 to 114, or the use of any one of claims ~~8283~~ to ~~85444~~, wherein the non-peptide linker comprises a linear 6 carbon chain linker.

116. The ~~method~~method of claim 82 or claims 86 to 115, or the use of any one of claims ~~8283~~ to ~~85445~~, wherein a composition or a mixture comprises the fusion construct and the checkpoint inhibitor.

117. The method of claim 82 or claims 86 to 116, or the use ~~method~~ of any one of claims ~~8283~~ to ~~44685~~, further comprising ~~contacting the cell, or administering,~~ an alkylating agent, anti-metabolite, plant extract, plant alkaloid, nitrosourea, hormone, nucleoside or a nucleotide analog, which is to be contacted with a cell or which is to be administered to the subject.

118. The ~~method~~method of claim 82 or claims 86 to 117, or the use of any one of claims ~~8283~~ to ~~85447~~, further comprising ~~contacting the cell, or administering,~~ an cyclophosphamide, azathioprine, cyclosporin A, prednisolone, melphalan, chlorambucil, mechlorethamine, busulfan, methotrexate, 6-mercaptopurine, thioguanine, 5-fluorouracil, cytosine arabinoside, AZT, 5-azacytidine (5-AZC), bleomycin, actinomycin D, mithramycin, mitomycin C, carmustine, lomustine, semustine, streptozotocin, hydroxyurea, cisplatin, carboplatin, oxiplatin, mitotane, procarbazine, dacarbazine, taxol (paclitaxel), vinblastine, vincristine, doxorubicin, dibromomannitol, irinotecan, topotecan, etoposide, teniposide, gemcitabine, pemetrexed, or a PARP inhibitor, which is to be contacted with a cell or which is to be administered to the subject.

119. The method of claim 82 or claims 86 to 118, or the use ~~method~~ of any one of claims ~~8283~~ to ~~85448~~, wherein the cell, hyperproliferation disorder or cancer is an ovarian cancer, breast cancer, melanoma or hepatocellular carcinoma.

120. The method of claim 82 or claims 86 to 119, or the use ~~method~~ of any one of claims ~~8283~~ to ~~85449~~, wherein the checkpoint inhibitor is an inhibitor or antagonist of PD-L1, PD-1 or CTLA-4.

121. The method of claim 82 or claims 86 to 120, or the use ~~method~~ of any one of claims ~~8283~~ to ~~85420~~, wherein the checkpoint inhibitor is an antagonist antibody that binds to PD-L1, PD-1 or CTLA-4.

122. The method of claim 82 or claims 86 to 121, or the use ~~method~~ of any one of claims ~~8283~~ to ~~85424~~, wherein the checkpoint inhibitor is selected from the group consisting of ipilimumab, atezolizumab, avelumab, durvalumab, cemiplimab, nivolumab and pembrolizumab.

123. ~~A method of treating a cancer in a subject, comprising administering to the subject~~ Use of a fusion construct and a checkpoint inhibitor in the manufacture of a medicament for treating an ~~in an amount sufficient to treat the~~ ovarian cancer or breast cancer,

wherein the fusion construct comprises a first lytic domain and a second domain, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1), KFAKFAKKFAKFAKKFA (SEQ. ID NO.3), KFAKFAKKFAKFAKKFAK(SEQ. ID NO.4), KFAKFAKKFAKFAKKFAKF (SEQ. ID NO.5) or KFAKFAKKFAKFAKKFAKFA (SEQ. ID NO.6); and the second domain comprises a luteinizing hormone releasing hormone (LHRH), an LHRH fragment, or an LHRH analog, ~~and~~

wherein the checkpoint inhibitor comprises an inhibitor an antagonist of PD-L1, PD-1 or CTLA-4, and wherein the cancer is selected from ovarian cancer, breast cancer, melanoma and hepatocellular carcinoma, ~~and~~

wherein the medicament is to be administered to a subject.

124. The ~~method~~use of claim 123, wherein the fusion construct comprises the amino acid sequence KFAKFAKKFAKFAKKFAKQHW SYGLRPG.

125. The ~~method~~use of claim 123 or 124, wherein the checkpoint inhibitor comprises an antagonist antibody that binds to PD-L1.

126. The ~~method~~use of claim 123 or 124, wherein the checkpoint inhibitor comprises an antagonist antibody that binds to CTLA-4.

127. The ~~method~~use of claim 123 or 124, wherein the checkpoint inhibitor comprises an antagonist antibody that binds to PD-1.

128. The ~~method~~use of claim 123 or 124, wherein the checkpoint inhibitor is selected from the group consisting of ipilimumab, atezolizumab, avelumab, durvalumab, cemiplimab, nivolumab and pembrolizumab.