

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), 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.
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), KFAKFAKKFAKFAKKFAKF (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), 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.
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 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 of 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 claims 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, cetrotorelix, ganirelix, abarelix, antide, teverelix and degarelix (Fe200486).

23. The method of anyone of claim 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 a fusion construct and a checkpoint inhibitor in an amount sufficient to treat the 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.

26. The method of claim 25, wherein 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.

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 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,

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.

28. The method of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy is metastatic, non-metastatic or benign.
29. The method of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy comprises a solid cellular mass.
30. The method of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy comprises hematopoietic cells.
31. The method 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 of claim 31, wherein the sarcoma comprises a lymphosarcoma, liposarcoma, osteosarcoma, chondrosarcoma, leiomyosarcoma, rhabdomyosarcoma or fibrosarcoma.
33. The method of claim 31, wherein the haematopoietic neoplasia, tumor, cancer or malignancy comprises a myeloma, lymphoma or leukemia.
34. The method 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 of claim 34, wherein the lung neoplasia, tumor, cancer or malignancy comprises ovarian cancer or melanoma.
36. The method of claim 26 or 27, wherein the neoplasia, tumor, cancer or malignancy comprises a stem cell neoplasia, tumor, cancer or malignancy.
37. The method of claim 26 or 27, wherein the method inhibits or reduces relapse or progression of the neoplasia, tumor, cancer or malignancy.
38. The method of claim 26 or 27, further comprising administering an anti-cell proliferative, anti-neoplastic, anti-tumor, anti-cancer or immune-enhancing treatment or therapy.
39. The method 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 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.

41. The method of claim 38, wherein 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, mitotane, procarbazine, dacarbazine, taxol, vinblastine, vincristine, doxorubicin, dibromomannitol or a PARP inhibitor.

42. The method of claim 38, wherein the treatment or therapy comprises administering a lymphocyte, plasma cell, macrophage, dendritic cell, NK cell or B-cell.

43. The method 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.

44. The method of claim 38, wherein 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 , 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.

45. The method of claim 38, wherein the fusion construct is 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 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 of any one of claims 25 to 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 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 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 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 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 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 of any one of claims 25 to 45, wherein the subject is a mammal.

54. The method 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 a fusion construct and a checkpoint inhibitor in an amount sufficient to treat 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.

56. The method of any one of claims 1 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 56, wherein the fusion construct has a smaller IC₅₀/(HA50, hemolytic activity) ratio, than Phor21- β CG-ala, Phor21-GSGGS- β CG-ala, Phor21-ASAAS- β CG-ala, or Phor14- β CG-ala.

58. The 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 of any one of claims 1 to 58, wherein the binding moiety has a linear or cyclic structure.
60. The method of any one of claims 1 to 59, 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 of any one of claims 1 to 60, wherein the first domain consists of a sequence from about 15 to about 20 amino acids.
62. The method of any one of claims 1 to 61, wherein the first domain consists of a sequence with 15, 16, 17, 18, 19 or 20 amino acids.
63. The method of any one of claims 1 to 62, wherein the second domain consists of or comprises an amino acid sequence set forth as: SYAVALSAQAALARR.
64. The method of any one of claims 1 to 63, wherein the second domain consists of or comprises an amino acid sequence set forth as: QHWSYGLRPG.
65. The method of any one of claims 1 to 64, wherein the first domain is positioned at the NH₂-terminus relative to the second domain.
66. The method of any one of claims 1 to 65, wherein the second domain is positioned at the NH₂-terminus relative to the first domain.
67. The method of any one of claims 1 to 66, wherein the first domain or the second domain has one or more D-amino acids.
68. The method of any one of claims 1 to 67, wherein the first domain has a D-amino acid at any K, F or A residue.
69. The method of any one of claims 1 to 68, wherein the first domain forms an amphipathic alpha-helix.
70. The method of any one of claims 1 to 69, wherein the first and second domains are joined by a covalent bond.
71. The method of any one of claims 1 to 70, wherein the first and second domains are joined by a peptide or a non-peptide linker.
72. The method of any one of claims 1 to 71, 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 of any one of claims 1 to 72, 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 of any one of claims 1 to 73, wherein the first and second domains are joined by peptide sequence comprising or consisting of: GSGGS, ASAAS, or CCCCCC.
75. The method of any one of claims 1 to 74, further comprising a third, fourth, fifth, sixth or seventh domain.

76. The method of any one of claims 1 to 75, wherein the fusion construct is isolated or purified.
77. The method of any one of claims 1 to 76, wherein the fusion construct comprises a mixture.
78. The method of any one of claims 1 to 77, 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 of any one of claims 1 to 78, wherein the checkpoint inhibitor is an antagonist antibody that binds to PD-L1, PD-1 or CTLA-4.
80. The method of any one of claims 1 to 79, wherein the checkpoint inhibitor is selected from the group consisting of ipilimumab, atezolizumab, avelumab, durvalumab, cemiplimab, nivolumab and pembrolizumab.
81. The method of any one of claims 1 to 80, wherein the fusion construct is 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 a fusion construct and a checkpoint 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.
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 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,

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.

85. 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,

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.

86. The method of any one of claims 82 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 any one of claims 82 to 86, wherein the first lytic domain is positioned at the NH₂-terminus relative to the second domain.

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

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

90. The method of any one of claims 82 to 89, wherein the first lytic domain has a D-amino acid at any K, F or A residue.

91. The method of any one of claims 82 to 90, wherein the first lytic domain forms an amphipathic alpha-helix.

92. The method of any one of claims 82 to 91, wherein the first lytic and second domains are joined by a covalent bond.

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

94. The method of any one of claims 82 to 93, wherein the peptide linker has a length from 1 to 25 amino acid residues.
95. The method of any one of claims 82 to 94, 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 of any one of claims 82 to 95, 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 of any one of claims 82 to 96, wherein the fusion construct is isolated or purified.
98. The method of any one of claims 82 to 97, wherein the fusion construct has greater anti-cell proliferative activity than Phor21- β CG-ala, Phor21-(SEQ. ID NO.10)- β CG-ala, Phor21-(SEQ. ID NO.11)- β CG-ala, or Phor14- β CG-ala, as ascertained by a lower IC₅₀ value.
99. The method of any one of claims 82 to 98, wherein the fusion construct has a smaller IC₅₀/HA₅₀ (hemolytic activity) ratio, than Phor21- β CG-ala, Phor21-(SEQ. ID NO. 10)- β CG-ala, Phor21-(SEQ. ID NO.11)- β CG-ala, or Phor14- β CG-ala.
100. The method of any one of claims 82 to 99, 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 of any one of claims 82 to 100, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKK (SEQ. ID NO.1).
102. The method of any one of claims 82 to 100, wherein the first lytic domain consists of peptide KFAKFAKKFAKFAKKFAK (SEQ. ID NO.4).
103. The method of any one of claims 82 to 100, wherein the LHRH analog comprises Lupron (leuprolide).
104. The method of any one of claims 82 to 100, wherein the LHRH analog comprises zoladex (goserelin).
105. The method of any one of claims 82 to 100, wherein the LHRH analog comprises supprelin (histrelin).
106. The method of any one of claims 82 to 100, wherein the LHRH analog comprises triptorelin.
107. The method of any one of claims 82 to 100, wherein the LHRH analog comprises buserelin.
108. The method of any one of claims 80 to 100, wherein the LHRH analog comprises cetorelix.
109. The method of any one of claims 82 to 100, wherein the LHRH analog comprises ganirelix.

110. The method of any one of claims 82 to 100, wherein the LHRH analog comprises abarelix.
111. The method of any one of claims 82 to 100, wherein the LHRH analog comprises antide.
112. The method of any one of claims 82 to 100, wherein the LHRH analog comprises teverelix.
113. The method of any one of claims 82 to 100, wherein the LHRH analog comprises degarelix (Fe200486).
114. The method of any one of claims 82 to 113, wherein the non-peptide linker comprises a linear carbon chain linker.
115. The method of any one of claims 82 to 114, wherein the non-peptide linker comprises a linear 6 carbon chain linker.
116. The method of any one of claims 82 to 115, wherein a composition or a mixture comprises the fusion construct and the checkpoint inhibitor.
117. The method of any one of claims 82 to 116, further comprising contacting the cell, or administering, an alkylating agent, anti-metabolite, plant extract, plant alkaloid, nitrosourea, hormone, nucleoside or a nucleotide analog.
118. The method of any one of claims 82 to 117, 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.
119. The method of any one of claims 82 to 118, wherein the cell, hyperproliferation disorder or cancer is an ovarian cancer, breast cancer, melanoma or hepatocellular carcinoma.
120. The method of any one of claims 82 to 119, wherein the checkpoint inhibitor is an inhibitor or antagonist of PD-L1, PD-1 or CTLA-4.
121. The method of any one of claims 82 to 120, wherein the checkpoint inhibitor is an antagonist antibody that binds to PD-L1, PD-1 or CTLA-4.
122. The method of any one of claims 82 to 121, 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 a fusion construct and a checkpoint inhibitor 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.

124. The method of claim 123, wherein the fusion construct comprises the amino acid sequence KFAKFAKKFAKFAKKFAKQHWSYGLRPG.

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

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

127. The method of any one of claims 123 to 124, wherein the checkpoint inhibitor comprises an antagonist antibody that binds to PD-1.

128. The method of any one of claims 123 to 124, wherein the checkpoint inhibitor is selected from the group consisting of ipilimumab, atezolizumab, avelumab, durvalumab, cemiplimab, nivolumab and pembrolizumab.