CLAIMS:

1. A chimeric Newcastle disease virus (NDV), comprising a packaged genome which encodes an agonist of a co-stimulatory receptor of an immune cell, wherein the co-stimulatory receptor is glucocorticoid-induced tumor necrosis factor receptor (GITR), inducible T-cell costimulator (ICOS), OX40, CD27, 4-1BB, CD226, cytotoxic and regulatory T cell molecule (CRTAM), death receptor 3 (DR3), lymphotoxin-beta receptor (LTBR), transmembrane activator and CAML interactor (TACI), B cell-activating factor receptor (BAFFR), B cell maturation protein (BCMA), LIGHT, or LT alpha, and wherein the agonist is expressed by the virus.

2. The chimeric NDV of claim 1, wherein the sequence encoding the agonist is inserted between two transcription units of the packaged genome.

3. The chimeric NDV of claim 1 or 2, wherein the agonist is an antibody that specifically binds to the co-stimulatory receptor.

4. The chimeric NDV of claim 1 or 2, wherein the agonist is a ligand that specifically binds to the co-stimulatory receptor.

5. The chimeric NDV of claim 1 or 2, wherein the agonist is an antibody specifically binds to GITR, OX40, CD27, or 4-1BB.

6. The chimeric NDV of claim 1 or 2, wherein the agonist of the co-stimulatory receptor is lymphotoxin alpha, LIGHT or CD70.

7. The chimeric NDV of claim 1 or 2, wherein the agonist is a monoclonal antibody, a camelized antibody or single chain Fv that specifically binds to GITR.

8. A chimeric Newcastle disease virus (NDV), comprising a packaged genome which encodes an F-fusion or an HN-fusion protein, wherein the F-fusion protein comprises the cytoplasmic and transmembrane domains of an NDV F protein and an antibody or ligand that binds to a co-stimulatory receptor of an immune cell, and wherein the HN-fusion protein comprises the cytoplasmic and transmembrane domains of an NDV HN protein and an antibody or ligand that binds to a co-stimulatory receptor of an immune cell, and wherein the co-stimulatory receptor is glucocorticoid-induced tumor necrosis factor receptor (GITR), inducible T-cell costimulator (ICOS), OX40, CD27, 4-1BB, CD226, cytotoxic and regulatory T cell molecule (CRTAM), death receptor 3 (DR3), lymphotoxin-beta receptor (LTBR), transmembrane activator and CAML interactor (TACI), B cell-activating factor receptor (BAFFR), B cell maturation protein (BCMA), LIGHT, or LT alpha.

9. The chimeric NDV of claim 8, wherein the sequence encoding the fusion protein is inserted between two transcription units of the packaged genome.

10. The chimeric NDV of claim 3, 5, 8, or 9, wherein the antibody is a monoclonal antibody, a camelized antibody, or a single-chain Fv.

11. The chimeric NDV of claim 4, 8, or 9, wherein the ligand is GITRL, HVEM, 4-1BBL, CD137L, OX40L, CD70, or ICOSL.

12. The chimeric NDV of any one of claims 1 to 11, wherein the packaged genome encodes a mutated F protein and the mutated F protein is expressed by the virus, wherein the mutated F protein comprises a mutated cleavage site.

13. The chimeric NDV of claim 12, wherein the mutated F protein causes the chimeric NDV to be highly fusogenic.

14. The chimeric NDV of any one of claims 1 to 11, wherein the packaged genome encodes a mutated F protein with the amino acid mutation L289A, wherein the mutated F protein is expressed by the chimeric NDV.

15. The chimeric NDV of any one of claims 1 to 14, wherein the chimeric NDV is lentogenic.

16. The chimeric NDV of claim 1 to 15, wherein the immune cell is a T lymphocyte or natural killer (NK) cell.

17. A pharmaceutical composition comprising the chimeric NDV of any one of claims 1 to 16, and a pharmaceutically acceptable carrier.

18. A method for producing a pharmaceutical composition, the method comprising:

a. propagating the chimeric NDV of any one of claims 1 to 16 in a cell line that is susceptible to a NDV infection; and

b. collecting the progeny virus,

wherein the virus is grown to sufficient quantities and under sufficient conditions that the virus is free from contamination, such that the progeny virus is suitable for formulation into a pharmaceutical composition.

19. A method for producing a pharmaceutical composition, the method comprising:

a. propagating the chimeric NDV of any one of claims 1 to 16 in an embryonated egg; and

b. collecting the progeny virus,

wherein the virus is grown to sufficient quantities and under sufficient conditions that the virus is free from contamination, such that the progeny virus is suitable for formulation into a pharmaceutical composition.

20. A cell line comprising the chimeric NDV of any one of claims 1 to 16.

21. An embryonated egg comprising the chimeric NDV of any one of claims 1 to 16.

22. The embryonated egg of claim 21, which is a chicken or quail egg.

23. Use of the chimeric NDV of any one of claims 1 to 16 for the preparation of a medicament for treating cancer in a subject in need thereof.

24. The use of claim 23, wherein the medicament is for administration to the subject in combination with a second agonist of a co-stimulatory receptor of an immune cell.

25. The use of claim 23, wherein the medicament is for administration to the subject in combination with an antagonist of an inhibitory receptor of an immune cell or its ligand.

26. Use of the pharmaceutical composition of claim 17 for the preparation of a medicament for treating cancer in a subject in need thereof.

27. The use of any one of claims 23 to 26 further in combination with the administration of adoptive T lymphocytes.

28. The use of any one of claims 23 to 27, wherein the cancer is melanoma, colorectal cancer, breast cancer, ovarian cancer, renal cell cancer, malignant melanoma, malignant glioma, renal cell carcinoma, pancreatic adenocarcinoma, malignant mesothelioma, lung adenocarcinoma, lung small cell carcinoma, lung squamous cell carcinoma, anaplastic thyroid cancer or head and neck squamous cell carcinoma.

29. The use of any one of claims 23 to 27, wherein the cancer is fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon cancer, colorectal cancer, kidney cancer, pancreatic cancer, bone cancer, breast cancer, ovarian cancer, prostate cancer, esophageal cancer, stomach cancer, oral cancer, nasal cancer, throat cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, uterine cancer, testicular cancer, cancer cell lung carcinoma, bladder carcinoma, lung cancer, epithelial carcinoma, glioma, glioblastoma multiforme, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, skin cancer, melanoma, neuroblastoma, or retinoblastoma.

30. The use of any one of claims 23 to 27, wherein the cancer is a leukemia, polycythemia vera, a lymphoma, a multiple myeloma, Waldenström's macroglobulinemia, monoclonal gammopathy of undetermined significance, benign monoclonal gammopathy, heavy chain disease, a bone and connective tissue sarcoma, a brain tumor, a breast cancer, an adrenal cancer, a thyroid cancer, a pancreatic cancer, a pituitary cancer, an eye cancer, a vaginal cancer, a vulvar cancer, a cervical cancer, a uterine cancer, an ovarian cancer, an esophageal cancer, a stomach cancer, a colon cancer, a rectal cancer, a liver cancer, a gallbladder cancer, a cholangiocarcinoma, a lung cancer, a testicular cancer, a penal cancer, an oral cancer, a basal cancer, a salivary gland cancer, a pharynx cancer, a skin cancer, a kidney, Wilms' tumor, a bladder cancer, myxosarcoma, osteogenic sarcoma, endotheliosarcoma, lymphangioendotheliosarcoma, mesothelioma, synovioma, hemangioblastoma, epithelial carcinoma, cystadenocarcinoma, bronchogenic carcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, or a papillary adenocarcinoma.

31. The use of claim 30, wherein

(a) the leukemia is acute leukemia, acute lymphocytic leukemia, an acute myelocytic leukemia, or a chronic leukemia,

(b) the lymphoma is Hodgkin's disease or non-Hodgkin's disease;

(c) the multiple myeloma is smoldering multiple myeloma, nonsecretory myeloma, osteosclerotic myeloma, placancer cell leukemia, solitary placancercytoma or extramedullary placancercytoma;

(d) the bone and connective tissue sarcoma is bone sarcoma, osteosarcoma, chondrosarcoma, Ewing's sarcoma, malignant giant cell tumor, fibrosarcoma of bone, chordoma, periosteal sarcoma, soft-tissue sarcomas, angiosarcoma (hemangiosarcoma), fibrosarcoma, Kaposi's sarcoma, leiomyosarcoma, liposarcoma, lymphangiosarcoma, neurilemmoma,

rhabdomyosarcoma, or synovial sarcoma;

(e) the brain tumor is glioma, astrocytoma, brain stem glioma, ependymoma, oligodendroglioma, nonglial tumor, glioblastoma multiforme, acoustic neurinoma, craniopharyngioma, medulloblastoma, meningioma, pineocytoma, pineoblastoma, or primary brain lymphoma;

(f) the breast cancer is ductal carcinoma, adenocarcinoma, lobular (cancer cell) carcinoma, intraductal carcinoma, medullary breast cancer, mucinous breast cancer, tubular breast cancer, papillary breast cancer, Paget's disease, or inflammatory breast cancer;

(g) the adrenal cancer pheochromocytom or adrenocortical carcinoma;

(h) the thyroid cancer is papillary or follicular thyroid cancer, medullary thyroid cancer, or anaplastic thyroid cancer;

(i) the pancreatic cancer is insulinoma, gastrinoma, glucagonoma, vipoma, somatostatin-secreting tumor, or carcinoid or islet cell tumor;

(j) the pituitary cancer is Cushing's disease, prolactin-secreting tumor, acromegaly, or diabetes insipidus;

(k) the eye cancer is ocular melanoma or retinoblastoma;

(l) the vaginal cancer is squamous cell carcinoma, adenocarcinoma, or melanoma;

(m) the vulvar cancer squamous cell carcinoma, melanoma, adenocarcinoma, basal cell carcinoma, sarcoma, or Paget's disease;

(n) the cervical cancer is squamous cell carcinoma or adenocarcinoma;

(o) the uterine cancer is endometrial carcinoma or uterine sarcoma;

(p) the ovarian cancer is ovarian epithelial carcinoma, borderline tumor, germ cell tumor, or stromal tumor;

(q) the esophageal cancer is squamous cancer, adenocarcinoma, adenoid

cystic carcinoma, mucoepidermoid carcinoma, adenosquamous carcinoma, sarcoma, melanoma, placancercytoma, verrucous carcinoma, or oat cell (cancer cell) carcinoma;

(r) the stomach cancer is adenocarcinoma, fungating (polypoid), ulcerating, superficial spreading, diffusely spreading, malignant lymphoma, liposarcoma, fibrosarcoma, or carcinosarcoma;

(s) the liver cancer is hepatocellular carcinoma or hepatoblastoma;

(t) the gallbladder cancer is adenocarcinoma;

(u) the cholangiocarcinoma is papillary, nodular, or diffuse;

(v) the lung cancer is non-cancer cell lung cancer, squamous cell carcinoma, adenocarcinoma, large-cell carcinoma, or small-cell lung cancer;

(w) the testicular cancer is germinal tumor, seminoma, anaplastic, classic, spermatocytic, nonseminoma, embryonal carcinoma, teratoma carcinoma, choriocarcinoma, or a prostate cancer;

(x) the oral cancer is squamous cell carcinoma;

(y) the salivary gland cancer is adenocarcinoma, mucoepidermoid carcinoma, or adenoidcystic carcinoma;

(z) the pharynx cancer is squamous cell cancer or verrucous;

(aa) the skin cancer is basal cell carcinoma, squamous cell carcinoma and melanoma, superficial spreading melanoma, nodular melanoma, lentigo malignant melanoma, or acral lentiginous melanoma;

(bb) the kidney cancer is renal cell carcinoma, adenocarcinoma, hypernephroma, fibrosarcoma, or transitional cell cancer; or

(cc) the bladder cancer is transitional cell carcinoma, squamous cell cancer, adenocarcinoma, or carcinosarcoma.

32. The use of any one of claims 23 to 31, wherein the cancer is metastatic.

33. The use of any one of claims 23 to 32, wherein the cancer is refractory or recurrent.

34. The use of any one of claims 23 to 33, wherein the chimeric NDV is formulated for intratumoral administration.

35. The use of any one of claims 23 to 34, wherein the subject is a human.