

[8a] In one aspect of the present disclosure, there is provided an isolated fusion protein comprising, in an N- to C- terminal orientation:

(i) a portion consisting of in an N- to C-terminal orientation:

(a) a soluble portion of an extracellular domain of a human TGF β type II
5 ~~cytokine~~-receptor;

(ii) —(b) an amino acid linker; and

(iii) —(c) an immunoglobulin (Ig) hinge region; and

(iv) an immunoglobulin (Ig) Fc domain;

wherein the amino acid linker consists of from 5-10 to 40 amino acid residues.

10 **[8b]** In another aspect of the present disclosure, there is provided a human TGF β type II
~~cytokine~~-binding protein comprising two fusion proteins disclosed herein, wherein each fusion
protein comprises an extracellular domain of a human TGF β type II ~~cytokine~~-receptor, wherein
the two fusion proteins are covalently linked together, and wherein the two extracellular
domains together define a binding site for binding a human TGF β type II cytokine.

15 **[8c]** In a further aspect of the present disclosure, there is provided an isolated nucleic acid
comprising a nucleotide sequence encoding the fusion protein disclosed herein.

[8d] In another aspect of the present disclosure, there is provided an expression vector
comprising the nucleic acid disclosed herein.

20 **[8e]** In a further aspect of the present disclosure, there is provided a host cell comprising the
expression vector disclosed herein.

[8f] In another aspect of the present disclosure, there is provided a pharmaceutical composition
comprising: (i) the expression vector disclosed herein; and (ii) at least one pharmaceutically
acceptable carrier or diluent.

25 **[8g]** In a further aspect of the present disclosure, there is provided a use of a fusion protein
disclosed herein in the manufacture of a medicament for treating cancer in a subject in need
thereof.

WHAT IS CLAIMED IS:

1. An isolated fusion protein comprising, in an N- to C- terminal orientation:

(i) a portion consisting of in an N- to C-terminal orientation:

(i) (a) a soluble portion of an extracellular domain of a human TGF β type II
5 cytokine-receptor;

(ii) (b) an amino acid linker; and

(iii) (c) an immunoglobulin (Ig) hinge region; and

(iv)(ii) an immunoglobulin (Ig) Fc domain;

wherein the amino acid linker consists of from 5-10 to 40 amino acid residues.

10 ~~2. — The isolated fusion protein of claim 1, wherein the amino acid linker comprises from 10 to 40 amino acid residues.~~

~~32.~~ The isolated fusion protein of claim 1, wherein the amino acid linker consists of
~~comprises~~ from 10 to 30 amino acid residues.

15 ~~43.~~ The isolated fusion protein of claim 1, wherein the amino acid linker consists of
~~comprises~~ from 10 to 20 amino acid residues.

~~54.~~ The isolated fusion protein of claim 1, wherein the amino acid linker consists of
~~comprises~~ from 10 to 15 amino acid residues.

~~65.~~ The isolated fusion protein of any one of claims 1-~~54~~, wherein the amino acid linker
comprises a C-terminal portion of an immunoglobulin (Ig) C_H1 ~~CH1~~ domain.

20 ~~76.~~ The isolated fusion protein of claim ~~65~~, wherein the Ig C_H1 ~~CH1~~ domain is selected
from an IgG1, IgG2, IgG3, IgG4, IgA1, IgA2, IgD, IgE, and IgM C_H1 ~~CH1~~ domain.

~~87.~~ The isolated fusion protein of claim ~~76~~, wherein the Ig C_H1 ~~CH1~~ domain is an IgG1 C_H1
~~CH1~~ domain.

25 ~~98.~~ The isolated fusion protein of claim ~~87~~, wherein the amino acid linker comprises an
amino acid sequence selected from SEQ ID NO: 1, and SEQ ID NO: 60, ~~and SEQ ID NO: 61~~.

~~10. — The isolated fusion protein of any one of claims 1-9, wherein the cytokine receptor is a
human TGF β type II receptor.~~

~~1419~~. The isolated fusion protein of claim ~~10~~, wherein the soluble portion of an extracellular domain of a human TGF β type II cytokine-receptor comprises amino acid residues 23-159 of SEQ ID NO: 12.

~~14210~~. The isolated fusion protein of any one of claims 1-~~1419~~, wherein the Ig Fc domain and hinge region are selected from a human IgG1, IgG2, IgG3, IgG4, IgA1, IgA2, IgD, IgE, and IgM Fc domain and hinge region.

~~14311~~. The isolated fusion protein of claim ~~14210~~, wherein the Ig Fc domain and hinge region are a human IgG1 Fc domain and hinge region.

~~14412~~. The isolated fusion protein of claim ~~14311~~, wherein the Ig Fc domain and hinge region comprise the amino acid sequence of SEQ ID NO: 13.

~~14513~~. The isolated fusion protein of any one of claims 1-~~14412~~, wherein the Ig Fc, Ig hinge region, and Ig C_H1 ~~CH1~~-domain are derived from a single immunoglobulin.

~~14614~~. The isolated fusion protein of any one of claims 1-~~14513~~, wherein the fusion protein comprises an amino acid sequence selected from SEQ ID NO: 22, and SEQ ID NO: 62, ~~and~~ SEQ ID NO: 63.

~~14715~~. A human TGF β type II cytokine-binding protein comprising two fusion proteins of any one of claims 1-16, wherein each fusion protein comprises an extracellular domain of a human TGF β type II cytokine-receptor, wherein the two fusion proteins are covalently linked together, and wherein the two extracellular domains together define a binding site for binding a human TGF β type II cytokine.

~~14816~~. An isolated nucleic acid comprising a nucleotide sequence encoding the fusion protein of any one of claims 1-~~14715~~.

~~14917~~. An expression vector comprising the nucleic acid of claim ~~14816~~.

~~2018~~. The expression vector of claim ~~14917~~, wherein the expression vector is an oncolytic virus.

~~2419~~. The expression vector of claim ~~2018~~, wherein the oncolytic virus is an adenovirus.

~~2220~~. The expression vector of claim ~~2419~~, wherein the adenovirus is a type 5 adenovirus .

~~23~~21. The expression vector of claim ~~22~~20, wherein the nucleotide sequence encoding the fusion protein is inserted into an E1b-19K insertion site located between the start site of E1b-19K and the start site of E1b-55K.

5 ~~24~~22. The expression vector of claims ~~22~~20 or ~~23~~21, wherein the adenovirus comprises a deletion of a Pea3 binding site, or a functional fragment thereof.

~~25~~23. A host cell comprising the expression vector of any one of claims ~~19~~17-~~24~~22.

~~26~~24. A pharmaceutical composition comprising: (i) the expression vector of any one of claims ~~19~~17-~~24~~23; and (ii) at least one pharmaceutically acceptable carrier or diluent.

10 ~~27~~25. Use of a fusion protein of any one of claims 2-~~16~~14 in the manufacture of a medicament for treating cancer in a subject in need thereof.

~~28~~26. Use of an expression vector comprising an isolated nucleic acid comprising a nucleotide sequence encoding the fusion protein of any one of claims 2-~~17~~15 in the manufacture of a medicament for treating cancer in a subject in need thereof.

15 ~~29~~27. The use of claim ~~27~~25 or ~~28~~26, wherein the cancer is selected from melanoma, squamous cell carcinoma of the skin, basal cell carcinoma, head and neck cancer, breast cancer, anal cancer, cervical cancer, non-small cell lung cancer, mesothelioma, small cell lung cancer, renal cell carcinoma, prostate cancer, gastroesophageal cancer, colorectal cancer, testicular cancer, bladder cancer, ovarian cancer, liver cancer, hepatocellular carcinoma, cholangiocarcinoma, brain and central nervous system cancer, thyroid cancer, parathyroid
20 cancer (*e.g.*, parathyroid carcinoma), endometrial cancer, neuroendocrine cancer, lymphoma (*e.g.*, Hodgkin and non-Hodgkin), leukemia, merkel cell carcinoma, gastrointestinal stromal tumors, multiple myeloma, uterine cancer, a sarcoma, kidney cancer, ocular cancer, pancreatic cancer, and a germ cell cancer (*e.g.*, ovarian germ cell cancer).

25 ~~30~~28. The fusion protein of any one of claims 2-~~16~~15 or an expression vector comprising an isolated nucleic acid comprising a nucleotide sequence encoding the fusion protein of any one of claims 2-~~17~~15, for use in treating cancer.