CLAIMS

1. A fusosome composition comprising a plurality of fusosomes derived from a source cell, wherein the fusosomes of the plurality comprise:

(a) a lipid bilayer,

(b) a lumen comprising cytosol, wherein the lumen is surrounded by the lipid bilayer,

(c) an exogenous or overexpressed fusogen disposed in the lipid bilayer, wherein the fusogen comprises a sequence chosen from, paramyxovirus F and G proteins or F and H proteins or F and HN proteins, or a derivative thereof, or any combination thereof, and

(d) a cargo; and wherein:

the fusosomes do not comprise a nucleus;

the amount of viral capsid protein in the fusosome composition is less than 1% of total protein in the fusosome composition; and

the plurality of fusosomes, when contacted with a target cell population in the presence of an inhibitor of endocytosis, delivers the cargo to at least 30% of the number of cells in the target cell population compared to cells in a reference target cell population not treated with the inhibitor of endocytosis when the plurality of fusosomes is contacted with the reference target cell population.

2. The fusosome composition of claim 1, which delivers at least 40%, 50%, 60%, 70%, or 80% more of the cargo to the target cell population compared to the reference target cell population.

3. The fusosome composition of claim 1 or 2, wherein less than 10% of the cargo enters the cells of the target cell population by endocytosis.

4. The fusosome composition of any of any of claims 1-3, wherein the inhibitor of endocytosis is an inhibitor of lysosomal acidification.

5. The fusosome composition of any of claims 1-4, wherein the cargo enters the cells of the target cell population through a dynamin-independent pathway, a lysosomal acidification-independent pathway, a macropinocytosis-independent pathway, or an actin- independent pathway.

6. The fusosome composition of any of the preceding claims, wherein the fusosomes of the plurality comprise a targeting moiety, wherein the targeting moiety is specific for a cell surface molecule on a target cell.

7. The fusosome composition of claim 6, wherein the targeting moiety is comprised by the fusogen or is comprised by a separate molecule.

8. The fusosome composition of any of claims 1-7, wherein, when the plurality of fusosomes are contacted with a cell population comprising cells of the target cell population and cells of a non-target cell population, the cargo is delivered to at least 10-fold more target population cells than non-target population cells, or at least 10-fold more of the cargo is delivered to cells of the target cell population compared to cells of the reference target cell population.

9. The fusosome composition of any of claims 1-8, wherein the fusosomes of the plurality fuse at a higher rate with a target cell than with a non-target cell or a reference cell, by at least 50%.

10. The fusosome composition of any of claims 6-9, wherein the cell surface marker is a cell surface marker of a skin cell, a cardiomyocyte, a hepatocyte, an intestinal cell, a pancreatic cell, a brain cell, a prostate cell, a lung cell, a colon cell, or a bone marrow cell.

~~11. The fusosome composition of claim 10, wherein the re-targeted fusogen comprises a rhabdoviridae fusogen, a filoviridae fusogen, an arenaviridae fusogen, a togaviridae fusogen, a flaviviridae fusogen, a bunyaviridae fusogen, a hapadnaviridae fusogen, or a derivative thereof.~~

11~~12~~. The fusosome composition of any of claims 1-10~~11~~, wherein the fusosomes of the plurality comprise exosomes, microvesicles, or a combination thereof.

12~~13~~. The fusosome composition of any of claims 1-11~~12~~, wherein the fusosomes of the plurality have an average size of at least 50 nm, 100 nm, 200 nm, 500 nm, 1000 nm, 1200 nm, 1400 nm, or 1500 nm in diameter.

13~~14~~. The fusosome composition of any of claims 1-11~~12~~, wherein the fusosomes of the plurality have an average size of less than 100 nm, 80 nm, 60 nm, 40 nm, or 30 nm in diameter.

14~~15~~. The fusosome composition of any of claims 1-13~~14~~, wherein the source cell is selected from the group consisting of a neutrophil, a HEK293 cell, a granulocyte, a mesenchymal stem cell, a bone marrow stem cell, an induced pluripotent stem cell, an embryonic stem cell, a myeloblast, a myoblast, a hepatocyte, and a neuron.

15~~16~~. The fusosome composition of any of claims 1-14~~15~~, wherein the fusosomes of the plurality comprise a cytobiologic or an enucleated cell.

~~17. The fusosome composition of any of claims 1-16, wherein the fusogen is a mammalian fusogen.~~

~~18. The fusosome composition of any of claims 1-16, wherein the fusogen is a viral fusogen.~~

16~~19~~. The fusosome composition of any of claims 1-15~~18~~, wherein the fusogen is active at a pH of between 4 and 5, between 5 and 6, between 6 and 7, between 7 and 8, between 8 and 9, or between 9 and 10.

17~~20~~. The fusosome composition of any of claims 1-15~~18~~, wherein the fusogen is not active at a pH of between 4 and 5, between 5 and 6, between 6 and 7, between 7 and 8, between 8 and 9, or between 9 and 10.

~~21. The fusosome composition of any of claims 1-20, wherein the fusogen is a protein fusogen.~~

18~~22~~. The fusosome composition of any of claims 1-17~~21~~, wherein the fusogen comprises a Nipah virus protein F, a measles virus F protein, a tupaia paramyxovirus F protein, a paramyxovirus F protein, a Hendra virus F protein, a Henipavirus F protein, a

Morbilivirus F protein, a respirovirus F protein, a Sendai virus F protein, a rubulavirus F protein, an avulavirus F protein, or a derivative thereof; and/or

wherein the fusogen comprises a Nipah virus protein G, a measles protein H, a tupaia paramyxovirus H protein, a paramyxovirus G protein, a paramyxovirus H protein, a paramyxovirus HN protein, a Morbilivirus H protein, a respirovirus HN protein, a sendai HN protein, a rubulavirus HN protein, an avulavirus HN protein, or a derivative thereof.

1923. The fusosome composition of any of claims 1-1822, wherein the fusogen is present at a copy number of at least 10 copies per fusosome.

2024. The fusosome composition of any of claims 1-1923, wherein the fusogen comprises a sequence selected from the group consisting of Nipah virus F and G proteins, measles virus F and H proteins, tupaia paramyxovirus F and H proteins, paramyxovirus F and G proteins or F and H proteins or F and HN proteins, Hendra virus F and G proteins, Henipavirus F and G proteins, Morbilivirus F and H proteins, respirovirus F and HN protein, a Sendai virus F and HN protein, rubulavirus F and HN proteins, or avulavirus F and HN proteins, a derivative thereof, and any combination thereof.

2125. The fusosome composition of any of claims 1-2024, wherein the cargo comprises an exogenous protein or an exogenous nucleic acid.

2226. The fusosome composition of any of claims 1-2024, wherein the cargo comprises or encodes a cytosolic protein or a membrane protein.

2327. The fusosome composition of any of claims 1-2226, wherein the cargo comprises a therapeutic agent.

2428. The fusosome composition of any of claims 1-2327, wherein the cargo is present at a copy number of at least 1, 2, 5, 10, 20, 50, 100,200, 300, 400, 500, 600, 700, 800, or 900 copies per fusosome.

2529. The fusosome composition of any of claims 1-2428, wherein the ratio of the copy number of the fusogen to the copy number of the cargo is between 1000:1 and 1:1, between 500:1 and 1:1, between 250:1 and 1:1, between 150:1 and 1:1, between 100:1 and 1:1, between 75:1 and 1:1, between 50:1 and 1:1, between 25:1 and 1:1, between 20:1 and 1:1, between 15:1 and 1:1, between 10:1 and 1:1, between 5:1 and 1:1, between 2:1 and 1:1, or between 1:1 and 1:2.

2630. The fusosome composition of any of claims 1-2529, wherein one or more of:

a) ratio of fusogen to CD63 of 100:10,000, 500:5,000, 1,000:5,000, 2,000:4,000, 2,500:3,500, 2,900:2,930, 2,910:2,915, or 2,912; or

b) the fusosome composition has a ratio of protein cargo to CD63 of 5:35, 10:30, 15:25, 16:19, 18:19, or 18.6; or

c) less than 15%, 20%, or 25% of the protein in the fusosomes is exosomal protein.

2731. The fusosome composition of any of claims 1-2630, wherein one or more of:

a) the fusogen comprises 1-30%, 5-20%, 10-15%, 12-15%, 13-14%, or 13.6% of the total protein in the fusosomes;

b) the fusogen to GAPDH ratio is 20:120, 40:100, 50:90, 60:80, 65:75, 68:70, or 69;

c) the fusogen to CNX ratio is 200:900, 300:800, 400:700, 500:600, 520:590, 530:580, 540:570, 550:560, or 558.4;

d) at least 1%, 2%, 3%, 4%, 5%, 6%, 7% 8%, 9% or 10% of the protein in the fusosomes is ribosomal protein, or 1-20%, 3-15%, 5-12.5%, 7.5-11%, 8.5-10.5%, or 9- 10% of the protein in the fusosomes is ribosomal protein.

28~~32~~. A pharmaceutical composition comprising the fusosome composition of any of claims 1-27~~31~~ and a pharmaceutically acceptable carrier.

29~~33~~. Use of a pharmaceutical composition of claim 28~~32~~ in the manufacture of a medicament for delivering a therapeutic agent to a subject having a disease or disorder, wherein said disease or disorder is a cancer, an inflammatory disorder, autoimmune disease, a chronic disease, inflammation, damaged organ function, an infectious disease, a degenerative disorder, a genetic disease, or an injury.

30~~34~~. A method of manufacturing a fusosome composition, comprising:

a) providing a fusosome composition of any of claims 1-27~~31~~; and

b) formulating the fusosome composition as a pharmaceutical composition suitable for administration to a subject.

31~~35~~. A method of manufacturing a fusosome composition, comprising:

a) providing a fusosome composition of any of claims 1-27~~31~~; and

b) assaying one or more fusosomes of the plurality to determine the presence or level of one or more of the following factors: (i) an immunogenic molecule; (ii) a pathogen; or (iii) a contaminant; and

c) approving the plurality of fusosomes or the fusosome composition for release if the level of the one or more factors is below a reference value.