CLAIMS:

1. A fusosome comprising:

a) a lipid bilayer comprising a re-targeted paramyxoviral fusogen, wherein the fusogen is linked to a targeting moiety and the re-targeted fusogen leads to preferential delivery of an exogenous agent to a target cell compared to a non-target cell; and

b) a nucleic acid that comprises or encodes:

(i) a positive target cell- specific regulatory element operatively linked to a nucleic acid encoding ~~an~~ the exogenous agent, wherein the positive tissue-specific regulatory element increases expression of the exogenous agent in ~~a~~ the target cell ~~or tissue~~ relative to an otherwise similar fusosome lacking the positive tissue-specific regulatory element; or

(ii) a non-target cell- specific regulatory element operatively linked to the nucleic acid encoding the exogenous agent, wherein the non-target cell-specific regulatory element decreases expression of the exogenous agent in a non-target cell or tissue relative to an otherwise similar fusosome lacking the non-target cell-specific regulatory element.

2. A fusosome comprising:

a) a lipid bilayer comprising a re-targeted paramyxoviral fusogen, wherein the fusogen is linked to a targeting moiety and the re-targeted fusogen leads to preferential delivery of an exogenous agent to a target cell compared to a non-target cell; and

b) a nucleic acid that comprises or encodes:

(i) a positive target cell- specific regulatory element operatively linked to a nucleic acid encoding ~~an~~ the exogenous agent, wherein the positive tissue-specific regulatory element increases expression of the exogenous agent in a target cell or tissue relative to an otherwise similar fusosome lacking the positive tissue-specific regulatory element; and

(ii) a non-target cell- specific regulatory element operatively linked to the nucleic acid encoding the exogenous agent, wherein the non-target cell-specific regulatory element decreases expression of the exogenous agent in a non-target cell or tissue relative to an otherwise similar fusosome lacking the non-target cell-specific regulatory element.

3. The fusosome of claim 1 or claim 2, wherein the fusosome comprises the exogenous agent or a nucleic acid encoding the exogenous agent.

4. The fusosome of any of claims 1-3~~the preceding claims~~, wherein one or more of:

i) the fusosome fuses at a higher rate with a target cell than with a non-target cell, optionally wherein the higher rate is by at least at least 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 2-fold, 3-fold, 4-fold, 5-fold, l0-fold, 20-fold, 50-fold, or l00-fold;

ii) the fusosome fuses at a higher rate with a target cell than with another fusosome, optionally wherein the higher rate is by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, 2-fold, 3-fold, 4-fold, 5-fold, l0-fold, 20-fold, 50-fold, or l00-fold;

iii) the fusosome fuses with target cells at a rate such that the exogenous agent in the fusosome is delivered to at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, of target cells after 24, 48, or 72 hours;

iv) the fusosome delivers the nucleic acid to a target cell at a higher rate than to a non-target cell, optionally wherein the higher rate is by at least at least 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 2-fold, 3-fold, 4-fold, 5-fold, l0-fold, 20- fold, 50-fold, or l00-fold;

v) the fusosome delivers the nucleic acid to a target cell at a higher rate than to another fusosome, optionally wherein the higher rate is by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, 2-fold, 3-fold, 4-fold, 5-fold, l0-fold, 20-fold, 50-fold, or 100- fold; or

vi) the fusosome delivers the nucleic acid to a target cell at a rate such that the exogenous agent in the fusosome is delivered to at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, of target cells after 24, 48, or 72 hours.

5. The fusosome of any of claims 1-4~~the preceding claims~~, wherein, when the fusosome is administered to a subject, one or more of:

i) less than 10%, 5%, 4%, 3%, 2%, or 1% of the exogenous agent detectably present in the subject is in non-target cells;

ii) at least 90%, 95%, 96%, 97%, 98%, or 99% of the cells of the subject that detectably comprise the exogenous agent, are target cells, optionally wherein the target cells are of a single cell type, optionally wherein the target cells are T cells;

iii) less than 1,000,000, 500,000, 200,000, 100,000, 50,000, 20,000, or 10,000 cells of the cells of the subject that detectably comprise the exogenous agent are non-target cells;

iv) average levels of the exogenous agent in all target cells in the subject are at least 100-fold, 200-fold, 500-fold, or 1, 000-fold higher than average levels of the exogenous agent in all non-target cells in the subject; or

v) the exogenous agent is not detectable in any non-target cell in the subject.

~~6. The fusosome of any of the preceding claims, wherein the fusogen is a re-targeted fusogen.~~

6~~7~~. The fusosome of any of claims 1-5~~claim 6~~, wherein the re-targeted paramyxoviral fusogen comprises a sequence chosen from ~~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,~~ or a derivative thereof, or any combination thereof.

7. The fusosome of claim 6, wherein the re-targeted paramyxoviral fusogen comprises a sequence chosen from Nipah virus F and G proteins, measles virus F and H proteins, tupaia paramyxovirus F and H 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, or a derivative thereof, or any combination thereof.

8. The fusosome of claim 6, wherein the re-targeted paramyxoviral fusogen comprises a sequence of canine distemper virus.

9~~8~~. The fusosome of any of claims 1-8~~the preceding claims~~, wherein the re-targeted paramyxoviral fusogen comprises a domain of at least 100 amino acids in length having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity to a wild-type paramyxovirus fusogen, optionally wherein the wild-type paramyxovirus fusogen is set forth in any one of SEQ ID NOS: 1-132.

10~~9~~. The fusosome of claim 9~~8~~, wherein the wild-type paramyxovirus is a Nipah virus, optionally wherein the Nipah virus is a henipavirus.

11. The fusosome of claim 10, wherein the re-targeted paramyxoviral fusogen comprises a Nipah virus F and G protein.

12~~10~~. The fusosome of any of claims 1-11 ~~the preceding claims~~, wherein the positive target cell-specific regulatory element comprises a tissue- specific promoter, a tissue-specific enhancer, a tissue-specific splice site, a tissue-specific site extending half-life of an RNA or protein, a tissue- specific mRNA nuclear export promoting site, a tissue-specific translational enhancing site, or a tissue-specific post-translational modification site.

13~~11~~. The fusosome of any of claims 1-12 ~~the preceding claims~~, wherein the positive target cell-specific regulatory element comprises a tissue- specific promoter.

14. The fusosome of claims 12 or 13, wherein the tissue-specific promoter is a promoter that drives expression in a liver cell.

15. The fusosome of claim 14, wherein the liver cell is a hepatocyte.

16. The fusosome of any of claims 12-15, wherein the tissue-specific promoter is selected from the group comprising hAAT, ApoE.HCR-hAAT, enhanced transthyretin, TTR, Alb, Apoa2, Cyp3a4, LP1B, MIR122, hemopexin, HLP, and VEC.

17~~12~~. The fusosome of any of ~~the preceding~~ claims 1-16, wherein the non-target cell specific regulatory element comprises a tissue- specific miRNA recognition sequence, tissue-specific protease recognition site, tissue-specific ubiquitin ligase site, tissue-specific transcriptional repression site, or tissue-specific epigenetic repression site.

18~~13~~. The fusosome of any of claims 1-17 ~~the preceding claims~~, wherein the non-target cell specific regulatory element comprises a tissue- specific miRNA recognition sequence.

19~~14~~. The fusosome of claim 18~~claim 13~~, wherein the non-target cell specific regulatory element is situated or encoded within a transcribed region encoding the exogenous agent.~~,~~ ~~optionally~~

20. The fusosome of claim 19, wherein an RNA produced by the transcribed region comprises the tissue-specific miRNA recognition sequence within a UTR or coding region.

21~~15~~. The fusosome of any of claim 1-20~~the preceding claims~~, wherein the target cell is a cancer cell and the non-target cell is a non-cancerous cell.

22~~16~~. The fusosome of any of ~~the preceding~~ claims 1-21, wherein the exogenous agent is an exogenous polypeptide or exogenous RNA.

23. The fusosome of claim 22, ~~optionally~~ wherein the exogenous agent is a therapeutic agent.

24. The fusosome of any of claims 1-23, wherein the exogenous agent comprises a membrane protein.

25. The fusosome of claim 24, wherein the membrane protein comprises a chimeric antigen receptor (CAR), a T cell receptor, an integrin, an ion channel, a pore forming protein, a Toll-Like Receptor, an interleukin receptor, a cell adhesion protein, or a transport protein.

26~~17~~. The fusosome of claims 1-25~~any of the preceding claims~~, wherein the fusosome further comprises:

i) a first exogenous or overexpressed immunosuppressive protein on the lipid bilayer and a second exogenous or overexpressed immunosuppressive protein on the lipid bilayer;

ii) a first exogenous or overexpressed immunosuppressive protein on the lipid bilayer and a second immunostimulatory protein that is absent or present at reduced levels, optionally wherein the reduced level is by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, compared to a fusosome generated from an otherwise similar, unmodified source cell; or

iii) a first immunostimulatory protein that is absent or present at reduced levels, optionally wherein the reduced level by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, compared to a fusosome generated from an otherwise similar, unmodified source cell and a second immunostimulatory protein that is absent or present at reduced levels, optionally wherein

the reduced level is by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, compared to a fusosome generated from an otherwise similar, unmodified source cell.

2718. The fusosome~~method~~ of claim 2617, wherein, when administered to a subject, one or more of:

i) the fusosome does not produce a detectable antibody response, or antibodies against the fusosome are present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level;

ii) the fusosome does not produce a detectable cellular immune response, or a cellular immune response against the fusosome is present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level;

iii) the fusosome does not produce a detectable innate immune response, or the innate immune response against the fusosome is present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level;

iv) less than 10%, 5%, 4%, 3%, 2%, or 1% of fusosomes are inactivated by serum;

v) a target cell that has received the exogenous agent from the fusosome does not produce a detectable antibody response, or antibodies against the target cell are present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level; or

vi) a target cell that has received the exogenous agent from the fusosome does not produce a detectable cellular immune response, or a cellular response against the target cell is present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level.

~~19. A fusosome comprising:~~

~~a) a lipid bilayer comprising a fusogen, and~~

~~b) an exogenous agent or a nucleic acid encoding an exogenous agent; and~~

~~c) one or more of:~~

~~i) a first exogenous or overexpressed immunosuppressive protein on the lipid bilayer and a second exogenous or overexpressed immunosuppressive protein on the lipid bilayer;~~

~~ii) a first exogenous or overexpressed immunosuppressive protein on the lipid bilayer and a second immuno stimulatory protein that is absent or present at reduced~~

~~levels, optionally wherein the reduced level is by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, compared to a fusosome generated from an otherwise similar, unmodified source cell; or~~

~~iii) a first immunostimulatory protein that is absent or present at reduced levels, optionally wherein the reduced level is reduced by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, compared to a fusosome generated from an otherwise similar, unmodified source cell and a second immunostimulatory protein that is absent or present at reduced levels, optionally wherein the reduced level is reduced by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, compared to a fusosome generated from an otherwise similar, unmodified source cell;~~

~~wherein, when administered to a subject, optionally wherein the subject is a human subject or a mouse, one or more of:~~

~~i) the fusosome does not produce a detectable antibody response, or antibodies against the fusosome are present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level;~~

~~ii) the fusosome does not produce a detectable cellular immune response, or a cellular immune response against the fusosome is present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level;~~

~~iii) the fusosome does not produce a detectable innate immune response, or the innate immune response against the fusosome is present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level;~~

~~iv) less than 10%, 5%, 4%, 3%, 2%, or 1% of fusosomes are inactivated by serum;~~

~~v) a target cell that has received the exogenous agent from the fusosome does not produce a detectable antibody response, or antibodies against the target cell are present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level; or~~

~~vi) a target cell that has received the exogenous agent from the fusosome does not produce a detectable cellular immune response, or a cellular response against the target cell is present at a level of less than 10%, 5%, 4%, 3%, 2%, or 1% above a background level.~~

28~~20~~. The fusosome of claim 27~~18 or claim 19~~, wherein the background level is the corresponding level in the same subject prior to administration of the fusosome.

29~~21~~. The fusosome of claim 27 or claim 28~~any one of claims 17-20~~, wherein the immunosuppressive protein is a complement regulatory protein or CD47.

30~~22~~. The fusosome of any of claims 21-23~~one of claims 18-21~~, wherein the immunostimulatory protein is an MHC~~, optionally wherein the MHC is an HLA,~~ protein.

31. The fusosome of claim 30, wherein the MHC protein is an HLA protein that is an HLA-G or HLA-E or a combination thereof.

~~23. A fusosome, comprising:~~

~~a) a lipid bilayer comprising a fusogen, and~~

~~b) a nucleic acid encoding an exogenous agent;~~

~~c) an exogenous or overexpressed MHC, optionally wherein the MHC is an HLA, optionally wherein the HLA is an HLA-G or HLA-E, or a combination thereof, on the lipid bilayer.~~

~~24. The fusosome of any one of claims 19-23, wherein the fusogen comprises a domain of at least 100 amino acids in length having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity to a wild-type paramyxovirus fusogen set forth in any one of SEQ ID NOS: 1-132.~~

~~25. A fusosome comprising:~~

~~a) a lipid bilayer comprising a fusogen, wherein the fusogen comprises a domain of at least 100 amino acids in length having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity to a wild-type paramyxovirus fusogen set forth in any one of SEQ ID NOS: 1-132;~~

~~b) a nucleic acid encoding an exogenous agent; and~~

~~c) an exogenous or overexpressed CD47 or a complement regulatory protein, or a combination thereof, on the lipid bilayer.~~

~~26. A fusosome comprising:~~

~~a) a lipid bilayer comprising a fusogen, wherein the fusogen comprises a domain of at least 100 amino acids in length having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99%~~

~~sequence identity to a wild-type paramyxovirus fusogen set forth in any one of SEQ ID NOS: 1-132, and~~

~~b) a nucleic acid encoding an exogenous agent; and~~

~~c) MHC I, optionally wherein the MHC I is HLA-A, HLA-B, or HLA-C, or MHC II, optionally wherein MHC II is HLA-DP, HLA-DM, HLA-DOA, HLA-DOB, HLA-DQ, or HLA-DR, that is absent or present at reduced levels, optionally wherein the reduced level is, reduced by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, compared to a fusosome generated from an otherwise similar, unmodified source cell.~~

~~27. A fusosome comprising:~~

~~a) a lipid bilayer comprising a fusogen, wherein the fusogen comprises a domain of at least 100 amino acids in length having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity to a wild-type paramyxovirus fusogen set forth in any one of SEQ ID NOS: 1-132; and~~

~~b) a nucleic acid encoding an exogenous agent; and~~

~~c) one or both of an exogenous or overexpressed immunosuppressive protein or an immunostimulatory protein that is absent or present at reduced levels, optionally wherein the reduced level is reduced by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%, compared to a fusosome generated from an otherwise similar, unmodified source cell.~~

3228. The fusosome of any of ~~the preceding~~ claims 1-31, wherein the nucleic acid comprises ~~[[w]]~~ one or more insulator elements.

~~29. A fusosome comprising:~~

~~a) a lipid bilayer comprising a fusogen, wherein the fusogen comprises a domain of at least 100 amino acids in length having at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity to a wild-type paramyxovirus fusogen set forth in any one of SEQ ID NOS: 1-132; and~~

~~b) a nucleic acid encoding an exogenous agent, wherein the nucleic acid comprises one or more insulator elements.~~

3330. The fusosome of claim 32 ~~claim 28 or claim 29~~, wherein the nucleic acid comprises two insulator elements.

34. The fusosome of claim 33, ~~optionally~~ wherein the two insulator elements comprise a first insulator element upstream of a region encoding the exogenous agent and a second insulator element downstream of a region encoding the exogenous agent.

35. The fusosome of claim 34, ~~optionally~~ wherein the first insulator element and second insulator element comprise the same or different sequences.

36. The fusosome of any of claims 1-35, wherein the target cell is selected from the group comprising: a T cell, a CD3+ T cell, a CD4+ T cell, a CD8+ T cell, a hepatocyte, a haematopoietic stem cell, a CD34+ haematopoietic stem cell, a CD 105+ haematopoietic stem cell, a CD117+ haematopoietic stem cell, a CD 105+ endothelial cell, a B cell, a CD20+ B cell, a CD19+ B cell, a cancer cell, a CD133+ cancer cell, an EpCAM+ cancer cell, a CD19+ cancel cell, a Her2/Neu+ cancer cell, a GluA2+ neuron, a GluA4+ neuron, a NKG2D+ natural killer cell, a SLC1A3+ astrocyte, a SLC7A10+ adipocyte, or a CD30+ lung epithelial cell.

37. The fusosome of any of claims 1-36, wherein the targeting moiety comprises an antibody or an antigen-binding fragment thereof (e.g.,Fab, Fab', F(ab')2, Fv fragments, scFv antibody fragments, disulfide-linked Fvs (sdFv), a Fd fragment consisting of the VH and CH1 domains, linear antibodies, single domain antibodies such as sdAb (either VL or VH), nanobodies, or camelid VHH domains), an antigen-binding fibronectin type III (Fn3) scaffold such as a fibronectin polypeptide minibody.

38. The fusosome of any of claims 1-37, wherein the fusosome is a retroviral vector or particle.

39. The fusosome of any of claims 1-38, wherein the fusosome is a lentiviral vector or particle.

~~31. The fusosome of any one of claims 28-30, wherein variation in the median exogenous agent level in a sample of cells isolated after administration of the fusosome to the subject at a first timepoint is at least, less than, or about 10,000%, 5,000%, 2,000%, 1,000%, 500%, 200%, 100%, 50%, 20%, 10%, or 5% of the median exogenous agent level in a sample of cells isolated after administration of the fusosome to the subject at a second, later timepoint.~~

~~32. The fusosome of any one of claims 28-31, wherein at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90% of target cells in the subject detectably comprise the exogenous agent.~~

~~33. The fusosome of any one of claims 28-32, wherein at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90% of target cells in the subject that detectably comprised the exogenous agent at a first time point still detectably comprise the exogenous agent at a second, later timepoint.~~

~~34. The fusosome of any one of claims 28-33, which is not genotoxic or does not increase the rate of tumor formation in target cells.~~

~~35. The fusosome of any one of claims 19-34, wherein the exogenous agent is an exogenous polypeptide or an exogenous RNA, optionally wherein the exogenous agent is a therapeutic agent.~~

~~36~~40. A fusosome of any of claims 1-39 for use in a method of delivering an exogenous agent to a subject comprising administering to the subject a fusosome of any of the preceding claims, thereby delivering the exogenous agent to the subject~~, optionally wherein the subject is a human subject~~.

~~37~~41. A fusosome of any of claims 1-39 for use in a method of treatment of a disease or condition ~~modulating a function~~, in a subject~~, target tissue or target cellcomprising contacting the target tissue or the target cell a fusosome of any of the preceding claims, optionally wherein the subject is a human subject~~.

~~38. The method of claim 37, wherein the target tissue or the target cell is present in a subject.~~

~~39. The method of claims 37 or claim 38, wherein the contacting is carried out by administering the fusosome to the subject.~~

~~40. A method of treating or preventing a disorder, in a subject, comprising administering to the subject a fusosome of any one of the preceding claims, optionally wherein the subject is a human subject.~~

42 Use of a fusosome of any of claims 1-39 for manufacture of a medicament for treating a disease or condition in a subject.

43. The fusosome of claim 40 or claim 41 or the use of claim 42, wherein the subject is a human subject.

~~44~~41. A method of making a fusosome of any of claims 1-39 ~~one of the preceding claims~~, comprising:

a) providing a cell that comprises the nucleic acid and the retargeted paramyxoviral fusogen ~~(e.g., re-targeted fusogen)~~;

b) culturing the cell under conditions that allow for production of the fusosome, and

c) separating, enriching, or purifying the fusosome from the cell, thereby making the fusosome.

~~42. A source cell for producing a fusosome, comprising:~~

~~a) a nucleic acid;~~

~~b) structural proteins that can package the nucleic acid, wherein at least one structural protein comprises a fusogen that binds a fusogen receptor; and~~

~~c) a fusogen receptor that is absent or present at reduced levels (e.g., reduced by at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90%) compared to an otherwise similar, unmodified source cell.~~

~~43. The source cell of claim 42, wherein the fusogen causes fusion of the fusosome with the target cell upon binding to the fusogen receptor.~~

~~44. The source cell of claim 42 or 43, which binds to the second similar source cell.~~, ~~e.g., the fusogen of the source cell binds to the fusogen receptor on the second source cell.~~

~~45. A population of source cells of any one of claims 42-44.~~

~~46. The population of source cells of claim 45, wherein less than 10%, 5%, 4%, 3%, 2%, or 1% of cells in the population are multinucleated.~~