BRIEF SUMMARY

[0004a] In one aspect, provided herein is a modified oncolytic virus comprising: an exogenous nucleic acid encoding a fusion protein comprising a metabolic modulating protein or a functional fragment or a variant thereof, wherein the exogenous nucleic acid encoding for the fusion protein comprises: a region encoding for IL-2 polypeptide or a functional fragment thereof; and a region encoding for leptin polypeptide leptin or a functional fragment thereof; an exogenous nucleic acid encoding a chemokine receptor or a functional fragment or a variant thereof, wherein the chemokine receptor is CCR2; and a genetic modification in a viral genome of the modified oncolytic virus.

[0004b] In another aspect, provided herein is a pharmaceutical composition comprising the modified oncolytic virus as described herein.

[0004c] In another aspect, provided herein is use of the modified oncolytic virus as described herein or the pharmaceutical composition as described herein in the manufacture of a medicament for enhancing therapeutic effect of a modified oncolytic virus upon systemic delivery of the modified oncolytic virus to a subject, relative to a reference virus comprising a TK mutation but not the exogenous nucleic acid encoding the fusion protein or the exogenous nucleic acid encoding the chemokine receptor that is to be administered by systemic administration, and wherein the modified oncolytic virus as described herein, or the pharmaceutical composition as described herein is to be administered by systemic administration.

[0004d] In another aspect, provided herein is use of the oncolytic virus as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for enhancing systemic immune response in a subject, wherein the oncolytic virus or the pharmaceutical composition that is to be administered results in an enhanced systemic immune response in the subject, relative to a reference oncolytic virus that comprises a deletion of a thymine kinase gene (TK-) and does not comprise the exogenous nucleic acid encoding a fusion protein comprising a metabolic modulating protein or functional fragment or variant thereof or the exogenous nucleic acid encoding the chemokine receptor or functional fragment or variant thereof that is to be administered to the subject.

[0004e] In another aspect, provided herein is the modified oncolytic virus as described herein or the pharmaceutical composition as described herein for use in therapy.

[0005] Provided herein are modified oncolytic vaccinia viruses comprising: an exogenous nucleic acid encoding a fusion protein comprising a metabolic modulating protein

or a functional fragment or a variant thereof, wherein the exogenous nucleic acid encoding for the fusion protein comprises: a polypeptide comprising IL-2 or a functional fragment thereof, and a polypeptide comprising leptin or a functional fragment thereof; an exogenous nucleic acid encoding a chemokine receptor or a functional fragment or a variant thereof, wherein the chemokine receptor is CCR2; and a genetic modification in a viral genome of the modified oncolytic virus. Further provided herein are modified oncolytic viruses, wherein the exogenous nucleic acid encoding the chemokine receptor comprises a codon optimized variant of the human coding sequence of the chemokine receptor. Further provided herein are modified oncolytic viruses, wherein the fusion protein further comprises a cytokine or a functional fragment or a variant thereof. Further provided herein are modified oncolytic viruses, wherein the genetic modification in the viral backbone is a mutation or a deletion of the A52R gene. Further provided herein are modified oncolytic viruses, wherein the deletion is a complete or a partial deletion. Further provided herein are modified oncolytic viruses, wherein the oncolytic virus further comprises a deletion of thymidine kinase gene. Further provided herein are modified oncolytic viruses, wherein the oncolytic virus comprises measles virus, poliovirus, poxvirus, vaccinia virus, an adenovirus, an adeno-associated virus, herpes simplex virus, vesicular stomatitis virus, reovirus, Newcastle disease virus, Seneca virus, lentivirus, mengovirus, or a myxoma virus. Further provided herein are modified oncolytic viruses, wherein the oncolytic virus is a pox virus. Further provided herein are modified oncolytic viruses, wherein the pox virus is a vaccina virus. Further provided herein are modified oncolytic viruses, wherein the vaccinia virus is a Western Reserve strain Vaccinia virus, a Copenhagen strain, an IHD strain, a Wyeth strain, a NYCBOH strain, a Tian Tan strain, a Lister strain, an Ankara strain, a USSR strain, an ACAM2000 strain, a Paris strain, a Bern strain, a Temple of Heaven strain, a Dairen strain, an EM-63 strain, an Evans strain, a King strain, a Patwadangar strain, or a Tash Kent strain. Further provided herein are modified oncolytic viruses, wherein the exogenous nucleic acid encoding the fusion protein is cloned into the locus of thymidine kinase gene. Further provided herein are modified oncolytic viruses, wherein the exogenous nucleic acid encoding the chemokine receptor is cloned into a locus of an A52R gene. Further provided herein are modified oncolytic viruses, wherein the polypeptide encoding IL-2 or a functional fragment thereof comprises a sequence that is at least about 75%, about 80%, about 85%, about 90%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% homologous to the sequence of SEQ ID NO: 4. Further provided herein are modified oncolytic viruses, wherein polypeptide encoding leptin or a functional fragment thereof comprises a sequence that is at least about 75%, about 80%, about 85%, about 90%, about 95%, about 96%, about 97%, about 98%, about 99%,