[0004a] In one aspect, provided herein is the use of a pharmaceutical composition in the manufacture of a medicament for the treatment of cancer, wherein the pharmaceutical composition comprises a therapeutic molecule selected from a library of therapeutic molecules, wherein the therapeutic molecule has been selected by a method comprising: modifying cancer cells from the subject to knock down or knock out the function of a plurality of genes, each gene in the plurality of genes encoding for a protein target of a therapeutic molecule in the library of therapeutic molecules, whereby the therapeutic molecule has been selected if knocking down or knocking out the function of the gene that encodes for the protein target of the selected therapeutic molecule impairs cancer cell viability.

[0004b] In another aspect, provided herein is the use of a pharmaceutical composition in the manufacture of a medicament for the treatment of cancer, wherein the pharmaceutical composition comprises a therapeutic molecule selected from a library of therapeutic molecules, wherein the cancer of the subject has been determined to be susceptible to the selected therapeutic molecule by a method comprising:

(a) contacting a sample of cancer cells from the subject with a library of gene modulatory reagents to generate a plurality of modified cancer cells, wherein each modified cancer cell harbors one or more of the gene modulatory reagents, and each gene modulatory reagent is capable of knocking down or knocking out the function of a gene that encodes a protein target of a therapeutic molecule in the library of therapeutic molecules; and

(b) sequencing the plurality of modified cancer cells, wherein a gene modulatory reagent that impairs cell viability will have fewer sequence reads than a gene modulatory reagent that does not impair cell viability, and the gene that is knocked down or knocked out by the gene modulatory reagent that impairs cell viability encodes for the protein targeted by the selected therapeutic molecule.

[0005] In one aspect, provided herein is a method of treating cancer in a subject in need thereof, the method comprising administering to the subject a therapeutic molecule selected from a library of therapeutic molecules; wherein the therapeutic molecule has been selected by a method comprising: modifying cancer cells from the subject to knock down or knock out the function of a plurality of genes, each gene in the plurality of genes encoding for a protein target of a therapeutic molecule in the library of therapeutic molecules, whereby the therapeutic molecule has been selected if knocking down or knocking out the function of the gene that encodes for the protein target of the selected therapeutic molecule impairs cancer cell viability. In some embodiments, the library of therapeutic molecules comprises at least 1, at least 2, at least 3, at least 4, at least 5, at least 10, or at least 20 therapeutic agents of Table 2. In some embodiments, the library of therapeutic molecules comprises at least 1, at least 2, at least 3, at least 4, at least 5, at least 10, or at least 20 therapeutic agents of Table 3. In some embodiments, one or more of the plurality of genes encode for a protein of Table 5B. In some embodiments, one or more of the plurality of genes encode for a protein of Table 5A. In some embodiments, one or more of the plurality of genes encode for a protein of Table 5C. In some embodiments, one or more of the plurality of genes encode for a protein of Table 5D. In some embodiments, one or more of the plurality of genes encode for a protein of Table 4. In some embodiments, one or more of the plurality of genes encode for a protein of Table 3.

[0006] In another aspect, provided herein is a method of treating cancer in a subject in need thereof, the

method comprising administering to the subject a therapeutic molecule selected from a library of therapeutic molecules; wherein the cancer of the subject has been determined to be susceptible to the selected therapeutic molecule by a method comprising: (a) contacting a sample of cancer cells from the subject with a library of gene modulatory reagents to generate a plurality of modified cancer cells, wherein each modified cancer cell harbors one or more of the gene modulatory reagents, and each gene modulatory reagent is capable of knocking down or knocking out the function of a gene that encodes a protein target of a therapeutic molecule in the library of therapeutic molecules, and (b) sequencing the plurality of modified cancer cells, wherein a gene modulatory reagent that impairs cell viability will have fewer sequence reads than a gene modulatory reagent that does not impair cell viability, and the gene that is knocked down or knocked out by the gene modulatory reagent that impairs cell viability encodes for the protein targeted by the selected therapeutic molecule. In some embodiments, prior to sequencing, one or more of the plurality of modified cancer cells have been propagated. In some embodiments, propagation comprises maintenance of the modified cancer cells in a 2D *in vitro* culture. In some embodiments, propagation comprises maintenance of the modified cancer cells in a 3D *in vitro* culture. In some embodiments, propagation comprises maintenance of the modified cancer cells *in vivo*. In some embodiments, propagation occurs within an animal model. In some embodiments, the animal is a rodent. In some embodiments, the cancer cells are primary cancer cells.

[0007] In some embodiments, contacting comprises introducing the one or more gene modulatory reagents into each cancer cell by a viral or non-viral delivery method. In some embodiments, one or more of the gene modulatory reagents in the library are encoded on a viral vector. In some embodiments, the viral vector comprises a lentiviral vector, adenoviral vector, or adeno-associated viral vector. In some