CLAIMS

What is claimed is:

1. Use of a therapeutically effective amount of a POLR2A inhibitor in the manufacture of a pharmaceutical composition for treating cancer in a patient, wherein cells of the cancer have been tested for: (i) a hemizygous loss of the TP53 gene; (ii) a hemizygous loss of the POLR2A gene; or (iii) a decreased level of expression of a POLR2A gene product relative to a reference expression level,
wherein the patient has been determined to have cancer cells that exhibit a decreased level of expression of a POLR2A gene product relative to an expression level in non-cancerous cells, and
wherein the POLR2A inhibitor comprises an amatoxin, and wherein the amatoxin is conjugated to an antibody which specifically binds to a tumor- associated antigen.

2. The use of claim 1, wherein the amatoxin is alpha-amanitin.

3. The use of claim 1, wherein the cancer cells exhibit a hemizygous loss of the TP53 gene or a hemizygous loss of the POLR2A gene.

4. The use of claim 1, wherein the cancer cells are lung cancer, brain cancer, breast cancer, liver cancer, ovarian cancer, colorectal cancer, prostate cancer, or pancreatic cancer cells.

5. The use of claim 1, wherein the cancer cells are metastatic, recurrent, or multidrug resistant.

6. Use of a therapeutically effective amount of a POLR2A inhibitor in the manufacture of a pharmaceutical composition for treating cancer in a patient, wherein

    (a) the patient is determined to have cancer cells comprising (i) a hemizygous loss of the TP53 gene; (ii) a hemizygous loss of the POLR2A gene; or (iii) a decreased level of expression of a POLR2A gene product relative to a reference level; and
    (b) the therapeutically effective amount of a POLR2A inhibitor is to be administered to the patient,

wherein the patient has been determined to have cancer cells that exhibit a decreased level of expression of a POLR2A gene product relative to an expression level in non-cancerous cells, and

wherein the POLR2A inhibitor comprises an amatoxin, and wherein the amatoxin is conjugated to an antibody which specifically binds to a tumor-associated antigen.

7. The use of claim 6, wherein the amatoxin is alpha-amanitin.

8. An in vitro method of selecting a drug therapy for a cancer patient comprising:

(a) detecting, in a sample of the cancer, the presence of (i) a hemizygous loss of the TP53 gene; (ii) a hemizygous loss of the POLR2A gene; or (iii) a decreased level of expression of a POLR2A gene product relative to a reference level in cells of the cancer; and

(b) selecting a POLR2A inhibitor if (i) a hemizygous loss of the TP53 gene is detected; (ii) a hemizygous loss of the POLR2A gene is detected; or (iii) a decreased level of expression of a POLR2A gene product relative to a reference level is detected in cells of the cancer,

wherein cells of the cancer are detected to have a decreased level of expression of a POLR2A gene product relative to an expression level in non-cancerous cells, and

wherein the POLR2A inhibitor comprises an amatoxin, and wherein the amatoxin is conjugated to an antibody which specifically binds to a tumor-associated antigen.

9. The method of claim 8, wherein cells of the cancer comprise a hemizygous loss of the TP53 gene or a hemizygous loss of the POLR2A gene.