CLAIMS

What is claimed is:

1. ~~A composition for use in treating a patient having a cancer, 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, the composition comprising~~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 POLR2A inhibitor comprises an amatoxin, and wherein the amatoxin is conjugated to an antibody which specifically binds to a tumor- associated antigen.

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

3. The ~~composition for~~ use of claim 1, wherein the reference expression level is an expression level in non-cancerous cells.

4. The ~~composition for~~ use of claim 1, wherein the cancer cells exhibit a hemizygous loss of the TP53 gene or a hemizygous loss of the POLR2A gene.

5. The ~~composition for~~ use of claim 1, wherein the patient has cancer cells that exhibit a decreased level of expression of a POLR2A gene product relative to a reference expression level.

6. The ~~composition for~~ 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.

7. The ~~composition for~~ use of claim 1, wherein the cancer cells are metastatic, recurrent, or multidrug resistant.

8. ~~The composition of any of claims 1 to 7 for use in a method of treating a patient having cancer comprising:~~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) ~~selecting 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) ~~administering a~~ the therapeutically effective amount of a POLR2A inhibitor is to be administered to the patient,

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 use of claim 8, wherein the amatoxin is alpha-amanitin.

~~9~~10. 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 the POLR2A inhibitor comprises an amatoxin, and wherein the amatoxin is conjugated to an antibody which specifically binds to a tumor-associated antigen.

~~10~~11. The method of claim ~~9~~10, wherein cells of the cancer comprise a hemizygous loss of the TP53 gene or a hemizygous loss of the POLR2A gene.

~~11~~12. The method of claim ~~9~~10, wherein cells of the cancer comprise a decreased level of expression of a POLR2A gene product relative to a reference level.