Claims

1. A combination comprising an oncolytic adenovirus, ~~and~~ a CDK4/6 inhibitor and at least one further agent selected from the group consisting of~~comprising~~ nutlin or a derivative of nutlin, ~~a PARP inhibitor,~~ a bromodomain inhibitor and a PARP inhibitor~~, nutlin or a derivative of nutlin~~.

2. The combination of claim 1, wherein the combination further comprises nutlin or a derivative of nutlin~~a PARP inhibitor~~.

3. The combination of any one of claims 1 and 2, wherein the combination further comprises a bromodomain inhibitor.

4. The combination of any one of claims 1 to 3, wherein the combination further comprises a PARP inhibitor~~nutlin or a nutlin derivative~~.

5. Use of a ~~The~~ combination of any one of claims 1 to 4 in the manufacture of a medicament ~~for use in a method~~ for the treatment of a tumor or cancer.

6. Use of a~~A~~n oncolytic adenovirus in the manufacture of a medicament ~~for use in a method~~ for the treatment of a tumor or cancer ~~in a subject~~, wherein the medicament is to be administered with ~~method comprises administering to the subject the adenovirus,~~ a CDK4/6 inhibitor and at least one further agent selected from the group consisting of ~~comprising~~ nutlin or a derivative of nutlin~~a PARP inhibitor~~, a bromodomain inhibitor and a PARP inhibitor~~, nutlin or a derivative of nutlin~~.

7. Use of a~~A~~ CDK4/6 inhibitor in the manufacture of a medicament ~~for use in a method~~ for the treatment of a tumor or cancer ~~in a subject~~, wherein the medicament is to be administered with ~~method comprises administering to the subject~~ an oncolytic adenovirus ~~, the CDK4/6 inhibitor~~ and at least one further agent selected from the group consisting of nutlin or a

derivative of nutlin, ~~comprising a PARP inhibitor,~~ a bromodomain inhibitor~~,~~ and a PARP inhibitor ~~nutlin or a derivative of nutlin~~.

8. Use of a nutlin or a derivative of nutlin in the manufacture of a medicament for the treatment of a tumor or a cancer, wherein the medicament is to be administered with an oncolytic adenovirus and a CDK4/6 inhibitor.

9. Use of a PARP inhibitor in the manufacture of a medicament for the treatment of a tumor or a cancer, wherein the medicament is to be administered with an oncolytic adenovirus and a CDK4/6 inhibitor.

10. Use of a bromodomain inhibitor in the manufacture of a medicament for the treatment of a tumor or a cancer, wherein the medicament is to be administered with an oncolytic adenovirus and a CDK4/6 inhibitor.

11~~8~~. The combination of any one of claims 1 to 4, and the use of any one of claims 5 to 10, ~~the combination for use of claim 5, the adenovirus for use of claim 6 and the CDK4/6 inhibitor for use of claim 7,~~ wherein the adenovirus is lacking expression of E1A13S~~an oncolytic adenovirus~~.

12~~9~~. The combination of any one of claims 1 to 4 and 11~~8~~, and the use of any one of claims 5 to 11~~the combination for use of any one of claims 5 and 8, the adenovirus for use of any one of claims 6 and 8, and the CDK4/6 inhibitor for use of any one of claims 7 and 8~~, wherein the adenovirus is selected from the group comprising XVir-N-31, dl520, AdΔ24, AdΔ24-RGD, dl922-947, E1Ad/01/07, dl1119/1131, CB 016, VCN-01, E1Adl1107, E1Adl1101, ORCA-010, and Enadenotucirev ~~and viruses lacking an expressed viral oncogene which is capable of binding a functional Rb tumor suppressor gene product~~.

13~~10~~. The combination of any one of claims 1 to 4 and 11~~8~~ to 12~~9~~, and the use of any one of claims 5 to 12~~the combination for use of any one of claims 5 and 8 to 9, the adenovirus for use of any one of claims 6 and 8 and 9, and the CDK4/6 inhibitor for use of any one of claims 7 to 9~~, wherein the adenovirus is XVir-N-31.

1411. The combination of any one of claims 1 to 4 and 118 to 1310, and use of any one of claims 5 to 13the combination for use of any one of claims 5 and 8 to 10, the adenovirus for use of any one of claims 6 and 8 to 10, and the CDK4/6 inhibitor for use of any one of claims 7 and 8 to 10, wherein the CDK4/6 inhibitor is a CDK4/6 inhibitor arresting cells in the G1 phase and inhibiting E2F1.

1512. The combination of any one of claims 1 to 4 and and 118 to 1411, and the use of any one of claims 5 to 14the combination for use of any one of claims 5 and 8 to 11, the adenovirus for use of any one of claims 6 and 8 to 11, and the CDK4/6 inhibitor for use of any one of claims 7 and 8 to 11, wherein the CDK4/6 inhibitor is selected from the group comprising palbociclib which is also referred to as PD 0332991, abemaciclib which is also referred to as LY-2835219, ribociclib which is also referred to as LEE011, Trilaciclib which is also referred to as G1T28, and Dinaciclib.

1613. The use of any one of claims 5 to 15combination for use of any one of claims 5 and 8 to 12, the adenovirus for use of any one of claims 6 and 8 to 12, and the CDK4/6 inhibitor for use of any one of claims 7 and 8 to 12, wherein the disease tumor or cancer is Rb-negative, .

14. The combination for use of any one of claims 5 and 8 to 12, the adenovirus for use of any one of claims 6 and 8 to 12, and the CDK4/6 inhibitor for use of any one of claims 7 and 8 to 12, wherein the disease tumor or cancer is expressing Rb or is Rb-positive.

1715. The use of any one of claims 5 to 16combination for use of any one of claims 5 and 8 to 14, the adenovirus for use of any one of claims 6 and 8 to 14, and the CDK4/6 inhibitor for use of any one of claims 7 and 8 to 14, wherein the cells of the tumor cells have a resistance to or are insensitive to one or several pharmaceutically active agents and/or radiation.

1816. The use of any one of claims 5 to 17combination for use of any one of claims 5 and 8 to 14, the adenovirus for use of any one of claims 6 and 8 to 14, and the CDK4/6 inhibitor for use of any one of claims 7 and 8 to 15, wherein the tumor or cancer contains YB-1 in the cell nucleus independent of the cell cycle.

19~~17~~. The use of any one of claims 5 to 18~~combination for use of any one of claims 5 and 8 to 15, the adenovirus for use of any one of claims 6 and 8 to 16, and the CDK4/6 inhibitor for use of any one of claims 7 and 8 to 16~~, wherein the tumor or cancer ~~disease~~ is selected from the group comprising bladder cancer, breast cancer, metastatic breast cancer (mBC), melanoma, glioma, pancreatic cancer, hepatocellular carcinoma, lung adenocarcinoma, sarcoma, ovarian cancer, renal cancer, prostate cancer, and leukemia.