## Claims

1. Use of nutlin-3 in the manufacture of a medicament for treating cancer in a patient, wherein said nutlin-3 is to be administered with VX-680,
wherein said nutlin-3 is to be administered prior to administration of said VX-680, and wherein said medicament selectively targets a p53-deficient cancer cell wherein said cancer is selected from the group consisting of leukemia; lymphoma; myeloma; skin cancer such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC) or melanoma; breast cancer; head and neck cancer, such as brain cancer; colorectal cancer; colon cancer; rectal cancer; lung cancer, such as non-small cell lung cancer; ovarian cancer; renal cancer; prostate cancer; liver cancer; and HPV- associated cancer such as cervical cancer.

2. The use according to claim 1, wherein said nutlin-3 is to be administered 12, 16, 18, 24, 36, 48 or 72 hours prior to administration of said VX-680.

3. A pharmaceutical combination for use in selectively targeting a p53-deficient cancer cell, in a patient suffering from cancer, comprising nutlin-3 and VX-680,
wherein said nutlin-3 is provided in a form suitable for administration prior to administration of said VX-680,
wherein said cancer is selected from the group consisting of leukemia; lymphoma; myeloma; skin cancer such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC) or melanoma; breast cancer; head and neck cancer, such as brain cancer; colorectal cancer; colon cancer; rectal cancer; lung cancer, such as non-

small cell lung cancer; ovarian cancer; renal cancer; prostate cancer; liver cancer; and HPV- associated cancer such as cervical cancer.

4. A method of identifying a cancer patient that is likely or not to respond to a therapy, comprising determining whether a cell or tissue sample isolated from the patient is p53-positive or p53-deficient, wherein determination that the cell or tissue sample is p53-deficient identifies the patient as likely to respond to the therapy, and wherein the therapy comprises administering to a patient nutlin-3 and VX-680,
wherein said nutlin-3 is to be administered prior to administration of said VX-680, and
wherein said cancer is selected from the group consisting of leukemia; lymphoma; myeloma; skin cancer such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC) or melanoma; breast cancer; head and neck cancer, such as brain cancer; colorectal cancer; colon cancer; rectal cancer; lung cancer, such as non-small cell lung cancer; ovarian cancer; renal cancer; prostate cancer; liver cancer; and HPV- associated cancer such as cervical cancer.

5. Use of nutlin-3 in the manufacture of a medicament for treating a cancer patient, wherein said nutlin-3 is to be administered with VX-680, wherein the patient is one who has been identified as likely to respond to the therapy, wherein the patient is identified by a method comprising determining whether a cell or tissue sample isolated from the patient is p53-positive or p53 deficient, wherein determination that the cell or tissue sample is p53 deficient identifies the patient as likely to respond to the therapy, and

wherein said nutlin-3 is to be administered prior to administration of said VX-680, and

wherein said cancer is selected from the group consisting of leukemia; lymphoma; myeloma; skin cancer such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC) or melanoma; breast cancer; head and neck cancer, such as brain cancer; colorectal cancer; colon cancer; rectal cancer; lung cancer, such as non-small cell lung cancer; ovarian cancer; renal cancer; prostate cancer; liver cancer; and HPV- associated cancer such as cervical cancer.

6. A kit for use in treating a cancer in a patient, the kit comprising:

i) nutlin-3,

ii) VX-680, and

iii) instructions to administer said nutlin-3 prior to administration of said VX-680;

wherein the cancer is p53-deficient cancer cells selected from the group consisting of leukemia; lymphoma; myeloma; skin cancer such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC) or melanoma; breast cancer; head and neck cancer, such as brain cancer; colorectal cancer; colon cancer; rectal cancer; lung cancer, such as non-small cell lung cancer; ovarian cancer; renal cancer; prostate cancer; liver cancer; and HPV- associated cancer such as cervical cancer.

7. A method for screening to identify a compound that selectively targets a first cell type or a second cell type, wherein the first cell type is a p53-deficient

cell and wherein the second cell type is a p53-positive cell, and wherein the first cell type is labelled with a first detectable marker and wherein the second cell type is labelled with a second detectable marker, the method comprising:

(i) contacting said first and second cell types with the compound; and

(ii) determining the relative amounts of the first and second detectable markers,

wherein the first and second detectable marker are independently detectable and wherein a relative increase in the amount of the first marker in comparison to the amount of the second marker is indicative of a compound selectively targeting a p53-positive cell and wherein a relative increase in the amount of the second marker is indicative of a compound selectively targeting a p53-deficient cell.

8. The method according to claim 7, wherein said detectable marker is selected from the group consisting of a fluorescent compound, a radioisotope compound, a non-radioisotope compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator compound, a chromogenic compound, an X-radiographic compound, and an enzyme.

9. The method according to claim 8, wherein said fluorescent compound is selected from the group consisting of a Green Fluorescent Protein (GFP), Red Fluorescent Protein (RFP), fluorescein, rhodamine, phycoerytherin, phycocyanin, allophycocyanin, o-phthaldehyde and fluorescamine.

10. The method according to claim 9, wherein said first cell type is labeled with RFP and said second cell type is labeled with GFP.

11. The method according to claim 7, wherein said cell types are contacted with the compound *in vitro, ex vivo* or *in vivo*.

12. The method of claim 7, wherein said relative amounts of the first and second marker are determined using fluorescence-activated cell sorting (FACS) or quantitative imaging microscopy.

## Claims

1. Use of nutlin-3 in the manufacture of a medicament for treating cancer in a patient, wherein said nutlin-3 is to be administered with VX-680,

   wherein said nutlin-3 is to be administered prior to administration of said VX-680, and wherein said medicament selectively targets a p53-deficient cancer cell.

2. The use according to claim 1, wherein said cancer is selected from the group consisting of leukemia; lymphoma; myeloma; skin cancer such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC) or melanoma; breast cancer; head and neck cancer, such as brain cancer; colorectal cancer; colon cancer; rectal cancer; lung cancer, such as non small cell lung cancer; ovarian cancer; renal cancer; prostate cancer; liver cancer; and HPV- associated cancer such as cervical cancer.

3. The use according to claim 1, wherein said nutlin-3 is to be administered 12, 16, 18, 24, 36, 48 or 72 hours prior to administration of said VX-680.

4. A pharmaceutical combination for use in selectively targeting a p53-deficient cancer cell, in a patient suffering from cancer, comprising nutlin-3 and VX-680,

   wherein said nutlin-3 is provided in a form suitable for administration prior to administration of said VX-680.

5. The combination according to claim 4, wherein said cancer is selected from the group consisting of leukemia; lymphoma; myeloma; skin cancer such as basal cell carcinoma (BCC), squamous cell carcinoma (SCC) or melanoma; breast cancer; head and neck cancer, such as brain cancer; colorectal cancer; colon cancer, rectal cancer; lung cancer, such as non small cell lung cancer; ovarian cancer; renal cancer; prostate cancer; liver cancer; and HPV- associated cancer such as cervical cancer.

6. A method of identifying a cancer patient that is likely or not to respond to a therapy, comprising determining whether a cell or tissue sample isolated from the patient is p53-positive or p53-deficient, wherein determination that the cell or tissue sample is p53-deficient identifies the patient as likely to respond to the therapy, and wherein the therapy comprises administering to a patient nutlin-3 and VX-680,

wherein said nutlin-3 is to be administered prior to administration of said VX-680.

7. Use of nutlin-3 in the manufacture of a medicament for treating a cancer patient, wherein said nutlin-3 is to be administered with VX-680, wherein the patient is one who has been identified as likely to respond to the therapy, wherein the patient is identified by a method comprising determining whether a cell or tissue sample isolated from the patient is p53-positive or p53 deficient, wherein determination that the cell or tissue sample is p53 deficient identifies the patient as likely to respond to the therapy, and

wherein said nutlin-3 is to be administered prior to administration of said VX-680.

8. A kit for use in selectively targeting p53-deficient cancer cells, in a patient suffering from cancer, the kit comprising:

i) nutlin-3,

ii) VX-680, and

iii) instructions to administer said nutlin-3 prior to administration of said VX-680.

9. A method for screening to identify a compound that selectively targets a first cell type or a second cell type, wherein the first cell type is a p53-deficient cell and wherein the second cell type is a p53-positive cell, and wherein the first cell type is labelled with a first detectable marker and wherein the second cell type is labelled with a second detectable marker, the method comprising:

(i) contacting said first and second cell types with the compound; and

(ii) determining the relative amounts of the first and second detectable markers,

wherein the first and second detectable marker are independently detectable and wherein a relative increase in the amount of the first marker in comparison to the amount of the second marker is indicative of a compound selectively targeting a p53-

positive cell and wherein a relative increase in the amount of the second marker is indicative of a compound selectively targeting a p53-deficient cell.

10. The method according to claim 9, wherein said detectable marker is selected from the group consisting of a fluorescent compound, a radioisotope compound, a non-radioisotope compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator compound, a chromogenic compound, an X-radiographic compound, and an enzyme.

11. The method according to claim 10, wherein said fluorescent compound is selected from the group consisting of a Green Fluorescent Protein (GFP), Red Fluorescent Protein (RFP), fluorescein, rhodamine, phycoerytherin, phycocyanin, allophycocyanin, o-phthaldehyde and fluorescamine.

12. The method according to claim 11, wherein said first cell type is labeled with RFP and said second cell type is labeled with GFP.

13. The method according to claim 9, wherein said cell types are contacted with the compound *in vitro, ex vivo* or *in vivo*.

14. The method of claim 9, wherein said relative amounts of the first and second marker are determined using fluorescence-activated cell sorting (FACS) or quantitative imaging microscopy.

15. An oral dosage form for use in cancer therapy, wherein said oral dosage form comprises

(i) a first composition comprising nutlin-3 for inducing cell cycle arrest in a p53-positive cell; and

(ii) a second composition comprising VX-680,

wherein said first composition is formulated for immediate release on contact with aqueous media and wherein said second composition is formulated for modified release on contact with aqueous media.

16. An oral dosage form as claimed in claim 15, wherein the first and second compositions are multiparticulates.

17. An oral dosage form as claimed in claim 16, wherein the multiparticulates comprising the first composition are uncoated and wherein the multiparticulates comprising the second composition have an enteric coat.

18. An oral dosage form as claimed in 16, wherein the multiparticulates are filled into a capsule.

19. An oral dosage form as claimed in claim 15 which takes the form of a tablet in which the first and second compositions are arranged in two or more separate layers.

20. An oral dosage form as claimed in claim 15, wherein the modified release comprises delayed and/or sustained release.

21. An oral dosage form as claimed in claim 15 in which the second composition is coated with an enteric coat.