

PHARMACEUTICAL COMPOSITIONS COMPRISING AZD5305

The present disclosure relates to pharmaceutical compositions suitable for oral administration, and more particularly to pharmaceutical tablets comprising the compound
5 known as "AZD5305" or a pharmaceutically acceptable salt thereof.

Background

PARP family of enzymes play an important role in a number of cellular processes, such as replication, recombination, chromatin remodeling, and DNA damage repair (O'Connor 2015).
10 Examples of PARP inhibitors and their mechanism of action are taught in e.g. WO2004/080976.

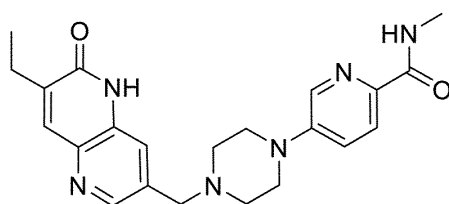
PARP1 and PARP2 are the most extensively studied PARPs for their role in DNA damage
15 repair. PARP1 is activated by DNA damage breaks and functions to catalyse the addition of poly (ADP-ribose) (PAR) chains to target proteins. This post-translational modification, known as PARylation, mediates the recruitment of additional DNA repair factors to DNA lesions.

20 Following completion of this recruitment role, PARP auto-PARylation triggers the release of bound PARP from DNA to allow access to other DNA repair proteins to complete repair. Thus, the binding of PARP to damaged sites, its catalytic activity, and its eventual release from DNA are all important steps for a cancer cell to respond to DNA damage caused by chemotherapeutic agents and radiation therapy (Bai 2015).

25 Inhibition of PARP family enzymes has been exploited as a strategy to selectively kill cancer cells by inactivating complementary DNA repair pathways. A number of pre-clinical and clinical studies have demonstrated that tumour cells bearing deleterious alterations of BRCA1 or BRCA2, key tumour suppressor proteins involved in double-strand DNA break
30 (DSB) repair by homologous recombination (HR), are selectively sensitive to small molecule inhibitors of the PARP family of DNA repair enzymes. Such tumours have deficient homologous recombination repair (HRR) pathways and are dependent on PARP enzymes function for survival. Although PARP inhibitor therapy has predominantly targeted *BRCA*-mutated cancers, PARP inhibitors have been tested clinically in non-*BRCA*-mutant tumors,
35 those which exhibit homologous recombination deficiency (HRD) (Turner 2004).

It is believed that PARP inhibitors having improved selectivity for PARP1 may possess improved efficacy and reduced toxicity compared to other clinical PARP1/2 inhibitors. It is believed also that selective strong inhibition of PARP1 would lead to trapping of PARP1 on DNA, resulting in DNA double-strand breaks (DSBs) through collapse of replication forks in S-phase. It is believed also that PARP1-DNA trapping is an effective mechanism for selectively killing tumour cells having HRD.

“AZD5305” refers to a compound with the chemical name 5-{4-[(7-ethyl-6-oxo-5,6-dihydro-1,5-naphthyridin-3-yl)methyl]piperazin-1-yl}-N-methylpyridine-2-carboxamide and structure shown below:



AZD5305 is a potent and selective PARP1 inhibitor and PARP1-DNA trapper with excellent *in vivo* efficacy. AZD5305 is highly selective for PARP1 over other PARP family members, with good secondary pharmacology and physicochemical properties and excellent pharmacokinetics in preclinical species, and with reduced effects on human bone marrow progenitor cells *in vitro*.

The synthesis of AZD5305 is described in Johannes 2021 and in WO2021/013735, the contents of which are hereby incorporated by reference in their entirety.

To deliver AZD5305 to patients, formulations need to be developed which are stable and have good dissolution properties.

Summary

- In some embodiments, disclosed is a pharmaceutical composition comprising:
- (a) from about 10.0 to about 25.0 wt% 5-{4-[(7-ethyl-6-oxo-5,6-dihydro-1,5-naphthyridin-3-yl)methyl]piperazin-1-yl}-N-methylpyridine-2-carboxamide (“AZD5305”), or a pharmaceutically acceptable salt thereof, measured as the free base;
 - (b) from about 0.5 to about 8.0 wt% of one of more pharmaceutical disintegrants;
 - (c) from about 0.5 to about 2.5 wt% of one or more pharmaceutical lubricants; and
 - (d) from about 64.5 to about 74.0 wt% of one or more pharmaceutical diluents

wherein the component weights, including any counterion from the pharmaceutical salt of AZD5305, if present, add up to 100.

In some embodiments, disclosed is a pharmaceutical tablet comprising the above
5 pharmaceutical composition. In some of these embodiments, the pharmaceutical tablet comprises a tablet core which comprises the pharmaceutical composition, and the tablet core has a coating.

In some embodiments, disclosed is a method of treatment or prophylaxis of diseases or
10 conditions in which inhibition of PARP1 is beneficial, comprising administering to the subject 5-{4-[(7-ethyl-6-oxo-5,6-dihydro-1,5-naphthyridin-3-yl)methyl]piperazin-1-yl}-N-methylpyridine-2-carboxamide ("AZD5305"), or a pharmaceutically acceptable salt thereof, in the form of a pharmaceutical composition or pharmaceutical tablet as disclosed herein.

15 In some embodiments, disclosed is 5-{4-[(7-ethyl-6-oxo-5,6-dihydro-1,5-naphthyridin-3-yl)methyl]piperazin-1-yl}-N-methylpyridine-2-carboxamide ("AZD5305"), or a pharmaceutically acceptable salt thereof, for use in a method of treatment or prophylaxis of diseases or conditions in which inhibition of PARP1 is beneficial, wherein said AZD5305, or
20 a pharmaceutically acceptable salt thereof, is administered in the form of a pharmaceutical composition or pharmaceutical tablet as disclosed herein.

In some embodiments, disclosed is the use of 5-{4-[(7-ethyl-6-oxo-5,6-dihydro-1,5-naphthyridin-3-yl)methyl]piperazin-1-yl}-N-methylpyridine-2-carboxamide ("AZD5305"), or a
25 pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in a method of treatment or prophylaxis of diseases or conditions in which inhibition of PARP1 is beneficial, wherein the medicament is a pharmaceutical composition or pharmaceutical tablet as disclosed herein.

30 In some embodiments, said disease or condition in which inhibition of PARP1 is beneficial is cancer. In some of these embodiments, the cancer is breast, ovary, pancreas, prostate, hematological, gastrointestinal such as gastric and colorectal, or lung cancer. In certain of these embodiments, the cancer is breast, ovary, pancreas or prostate cancer.

In some embodiments, the breast cancer is *BRCA1m* (*BRCA1* mutated), *BRCA2m* (*BRCA2* mutated), *PALB2m* (*PALB2* mutated), *RAD51Cm* (*RAD51C* mutated), or *RAD51Dm* (*RAD51D* mutated) HER2-negative breast cancer.

- 5 In some embodiments, the ovarian cancer is *BRCA1m* (*BRCA1* mutated), *BRCA2m* (*BRCA2* mutated), *PALB2m* (*PALB2* mutated), *RAD51Cm* (*RAD51C* mutated), or *RAD51Dm* (*RAD51D* mutated) ovarian cancer or ovarian cancer with high genomic instability.

- In some embodiments, the prostate cancer is *BRCA1/2* mutated prostate cancer or HRRm
10 (HRR mutated) non-*BRCA1/2* mutated prostate cancer.

Detailed Description

AZD5305

- In certain embodiments, the compositions described herein comprise AZD5305, or a
15 pharmaceutically acceptable salt thereof, in an amount from about 10.0 wt%, from about 11.0 wt%, from about 12.0 wt%, from about 13.0 wt%, from about 14.0 wt% , from about 15.0 wt%, from about 16.0 wt%, from about 17.0 wt%, from about 18.0 wt%, from about 19.0 wt%, from about 20.0 wt%, from about 21.0 wt%, from about 22.0 wt%, from about 23.0 wt%, or from about 24.0 wt%. The amount of AZD5305 may be up to about 25.0 wt%, up to
20 24.0 wt%, up to 23.0 wt%, up to 22.0 wt%, up to 21.0 wt%, up to 20.0 wt%, up to 19.0 wt%, up to 18.0 wt%, up to 17.0 wt%, up to 16.0 wt%, up to 15.0 wt%, up to 14.0 wt%, up to 13.0 wt%, up to 12.0 wt%, or up to about 11.0 wt%. The amount of AZD5305 in the composition is measured as the free base equivalent where it is present as pharmaceutically acceptable salt.

- 25 In certain embodiments, the compositions described herein AZD5305, or a pharmaceutically acceptable salt thereof, in an amount of about 10.0 wt%, 11.0 wt%, 12.0 wt%, 13.0 wt%, 14.0 wt% , 15.0 wt%, 16.0 wt%, 17.0 wt%, 18.0 wt%, 19.0 wt%, 20.0 wt%, 21.0 wt%, 22.0 wt%, 23.0 wt%, 24.0 wt%, or 25.0 wt%. The amount of AZD5305 in the composition is
30 measured as the free base equivalent where it is present as pharmaceutically acceptable salt.

- In one embodiment, the pharmaceutical composition comprises 20.0wt% of AZD5305, which may be present as a pharmaceutical salt thereof.

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In certain embodiments, the AZD5305 used in the compositions is in crystalline form.
In certain embodiments, the AZD5305 used in the compositions is in amorphous form.

In some embodiments, the AZD5305 may be present as a free base. In some embodiments, the AZD5305 is present as a pharmaceutically acceptable salt of AZD5305.

5 *Pharmaceutical disintegrants*

In this specification, the terms “disintegrant” and “disintegrants” are intended to be interpreted in the context of pharmaceutical formulation science. Accordingly, a disintegrant may be, for example: alginic acid, calcium alginate, carboxymethylcellulose calcium, chitosan, croscarmellose sodium, crospovidone, glycine, guar gum, hydroxypropyl cellulose, 10 low-substituted hydroxypropyl cellulose, magnesium aluminium silicate, methylcellulose, povidone, sodium alginate, sodium carboxymethylcellulose, sodium starch glycolate, starch, or a combination thereof.

Accordingly, in particular embodiments the one or more pharmaceutical disintegrants 15 comprises one or more pharmaceutical disintegrants selected from alginic acid, calcium alginate, carboxymethylcellulose calcium, chitosan, croscarmellose sodium, crospovidone, glycine, guar gum, hydroxypropyl cellulose, low-substituted hydroxypropyl cellulose, magnesium aluminium silicate, methylcellulose, povidone, sodium alginate, sodium carboxymethylcellulose, sodium starch glycolate and starch.

20 In some embodiments the one or more pharmaceutical disintegrants comprises one or more pharmaceutical disintegrants selected from alginic acid, calcium alginate, carboxymethylcellulose calcium, chitosan, croscarmellose sodium, crospovidone, glycine, guar gum, hydroxypropyl cellulose, low-substituted hydroxypropyl cellulose, magnesium 25 aluminium silicate, methylcellulose, povidone, sodium alginate, sodium carboxymethylcellulose and sodium starch glycolate.

In one embodiment, the one or more disintegrants is low-substituted hydroxypropyl cellulose.

30 In certain embodiments, the compositions described herein comprise one or more pharmaceutical disintegrants in an amount from about 0.5 wt%, from about 1.0 wt%, from about 2.0 wt%, from about 3.0 wt% or from about 4.0 wt%. The amount of the one or more pharmaceutical disintegrants may be up to about 8.0 wt%, up to 7.0 wt% or up to about 6.0 wt%.

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In certain embodiments, the compositions described herein comprise one or more pharmaceutical disintegrants in an amount of about 1.0 wt%, 2.0 wt%, 3.0 wt%, 4.0 wt%, 5.0 wt%, 6.0 wt% or 7.0 wt%.

- 5 In one embodiment, the pharmaceutical composition comprises 5.0wt% of one or more disintegrants which is low-substituted hydroxypropyl cellulose.

Pharmaceutical lubricants

- 10 The terms "lubricant" and "lubricants", as used herein, are intended to be interpreted in the context of pharmaceutical formulation science. Accordingly, a lubricant may be, for example calcium stearate, glyceryl behenate, glyceryl monostearate, glyceryl palmitostearate, a mixture of behenate esters of glycerine (e.g. a mixture of glyceryl bihenate, tribehenin and glyceryl behenate), leucine, magnesium stearate, myristic acid, palmitic acid, poloxamer, polyethylene glycol, potassium benzoate, sodium benzoate, sodium lauryl sulfate, sodium
- 15 stearate, sodium stearyl fumarate, stearic acid, talc, tribehenin and zinc stearate.

- Accordingly, in particular embodiments the one or more pharmaceutical lubricants comprises one or more pharmaceutical lubricants selected from calcium stearate, glyceryl behenate, glyceryl monostearate, glyceryl palmitostearate, a mixture of behenate esters of glycerine
- 20 (e.g., a mixture of glyceryl bihenate, tribehenin and glyceryl behenate), leucine, magnesium stearate, myristic acid, palmitic acid, poloxamer, polyethylene glycol, potassium benzoate, sodium benzoate, sodium lauryl sulfate, sodium stearate, sodium stearyl fumarate, stearic acid, talc, tribehenin and zinc stearate.

- 25 In other particular embodiments, the one or more pharmaceutical lubricants comprises one or more pharmaceutical lubricants selected from calcium stearate, glyceryl behenate, glyceryl monostearate, glyceryl palmitostearate, a mixture of behenate esters of glycerine (e.g., a mixture of glyceryl bihenate, tribehenin and glyceryl behenate), leucine, magnesium stearate, myristic acid, palmitic acid, poloxamer, polyethylene glycol, potassium
- 30 benzoate, sodium benzoate, sodium lauryl sulfate, sodium stearate, stearic acid, talc, tribehenin and zinc stearate.

- According to one embodiment of the disclosure, the one or more pharmaceutical lubricants comprises glyceryl behenate, magnesium stearate, stearic acid, or a combination thereof.

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In one embodiment, the lubricant is glyceryl behenate, magnesium stearate, or a combination thereof.

In one embodiment, the lubricant is magnesium stearate.

In certain embodiments, the compositions described herein comprise one or more
5 pharmaceutical lubricants in an amount from about 0.5 wt%, from about 1.0 wt%, from about 1.25 wt%, from about 1.5 wt% or from about 2.0 wt%. The amount of the one or more pharmaceutical lubricants may be up to about 2.5 wt%, up to 2.0 wt%, up to about 1.75 wt%, up to about 1.5 wt% or up to about 1.0 wt%.

10 In certain embodiments, the compositions described herein comprise one or more pharmaceutical lubricants in an amount of about 1.0 wt%, 1.25 wt%, 1.5 wt%, 1.75 wt% or 2.0 wt%.

In one embodiment, the pharmaceutical composition comprises 1.5wt% of one or more
15 lubricants which is magnesium stearate.

Pharmaceutical diluents

The pharmaceutical compositions of the present disclosure, in one embodiment, comprise one or more pharmaceutical diluents. The term "diluent" is used interchangeably herein with
20 "filler".

Suitable pharmaceutical diluents are known to those skilled in the art of pharmaceutical formulation science. Suitable pharmaceutical diluents, include, for example, microcrystalline cellulose, calcium carbonate, calcium phosphate, calcium hydrogen phosphate, calcium
25 sulfate, cellulose acetate, erythritol, ethylcellulose, fructose, inulin, isomalt, lactitol, lactose, magnesium carbonate, magnesium oxide, maltitol, maltodextrin, maltose, mannitol, polydextrose, polyethylene glycol, pullulan, simethicone, sodium bicarbonate, sodium carbonate, sodium chloride, sorbitol, starch, sucrose, trehalose and xylitol.

30 Accordingly, in particular embodiments the one or more pharmaceutical diluents comprises one or more pharmaceutical diluents selected from microcrystalline cellulose, calcium carbonate, calcium phosphate, calcium hydrogen phosphate, calcium sulfate, cellulose acetate, erythritol, ethylcellulose, fructose, inulin, isomalt, lactitol, lactose, magnesium carbonate, magnesium oxide, maltitol, maltodextrin, maltose, mannitol, polydextrose,
35 polyethylene glycol, pullulan, simethicone, sodium bicarbonate, sodium carbonate, sodium chloride, sorbitol, starch, sucrose, trehalose and xylitol.

In one embodiment, the one or more pharmaceutical diluents is microcrystalline cellulose. Microcrystalline cellulose is a binder/diluent in oral tablet and capsule formulations and can be used in dry-granulation, wet-granulation, and direct-compression processes.

- 5 In some embodiments, the pharmaceutical compositions of the present disclosure comprise two or more pharmaceutical diluents. In one of these embodiments, the two pharmaceutical diluents are microcrystalline cellulose and calcium hydrogen phosphate.

- 10 In certain embodiments, the compositions described herein comprise one or more pharmaceutical diluents in an amount from about 64.5 wt%, from about 65.0 wt%, from about 66.0 wt%, from about 67.0 wt%, from about 68.0 wt%, from about 69.0 wt%, from about 70.0 wt%, from about 71.0 wt%, from about 72.0 wt% or from about 73.0 wt%. The amount of the one or more pharmaceutical diluents may be up to about 73.0 wt%, up to 72.0 wt%, up to 71.0 wt%, up to 70.0 wt%, up to 69.0 wt%, up to 68.0 wt%, up to 67.0 wt%, up to 66.0 wt% or up to about 65.0 wt%.

- 15 In certain embodiments, the compositions described herein comprise one or more pharmaceutical diluents in an amount of about 64.5 wt%, 65.0 wt%, 66.0 wt%, 67.0 wt%, 68.0 wt%, 69.0 wt%, 70.0 wt%, 71.0 wt%, 72.0 wt%, 73.0 wt%, or 74.0 wt%.

- 20 In embodiment where there are two pharmaceutical diluents, they may be in a ratio of 1:1, 2:3, 1:2, 1:3 or 1:4. In some embodiments, they are in a ratio 1:3. In certain embodiments, the two pharmaceutical diluents are microcrystalline cellulose and calcium hydrogen phosphate, in a ratio of 3:1. This ratio has been found to provide good compaction properties, whilst maintaining solubility properties of the tablet. In particular embodiments, the pharmaceutical composition comprises 73.5 wt% of one or more diluents which are 55.0 wt% microcrystalline cellulose and 18.5 wt% calcium hydrogen phosphate.

Coating

- 30 In one embodiment, the composition provided herein is a tablet and has a film coating. The film coating may be applied using conventional methods known to those skilled in the art. A functional coating can be used to provide protection against, for example, moisture ingress or degradation by light, to colour the formulation. Additionally, a functional coating may be used to modify or control the release of AZD5305 from the composition.

- 35 Modified- and controlled-release coatings are known to those skilled in the art and include, for example, enteric coating (e.g., cellulose acetate phthalate, hydroxypropyl methylcellulose

phthalate, hydroxypropyl methylcellulose acetate succinate, polyvinyl acetate phthalate, pH-sensitive methacrylic acid/methylmethacrylate 30 copolymers, shellac, and mixtures thereof, reverse enteric coating (e.g., maltrin, aminoalkyl methacrylate copolymers available under the trade name of Eudragit® (type EI 00 or EPO), polyvinylacetal diethylaminoacetate e.g.,
5 AEA ® available from Sankyo Company Limited, Tokyo (Japan), and the like; and mixtures thereof) and water insoluble polymer coating (e.g., ethylcellulose, cellulose acetate, cellulose triacetate, cellulose acetate butyrate, polyvinyl acetate, neutral methacrylic acid-methylmethacrylate copolymers (e.g., Eudragit RL, RS, and NE30D, etc.), and mixtures thereof).

10

Suitable coatings, such as film coatings, that may be applied to the composition according to the disclosure comprise a film-forming agent, for example a sugar or more particularly a film-forming polymer. Suitable sugar coatings are well known to those skilled in the art and may comprise, for example, sucrose or lactose.

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In one embodiment, the film coating comprises a mixture of hypromellose, polyethylene glycol, titanium dioxide and iron oxide red, iron oxide yellow and iron oxide black, for example, the mixture sold under the trade name Aquarius Prime Brown BAP 312542 (Ashland).

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Other suitable film coatings are commercially available as concentrates that may be diluted with water and optionally a cellulose ether such as HPMC and a plasticizer such as polyethylene glycol prior to application to the composition. Such concentrates include Opaspray™ coatings from Colorcon, for example Opaspray™ Brown M- 1-25092 and
25 Opaspray Yellow M- 1-22842.

Suitable film-forming agents include, for example film-forming polymers, such as cellulose ethers, esters and mixed ethers and esters, including esters of water-soluble cellulose ethers, for example hydroxypropyl methylcellulose, hydroxypropyl ethylcellulose,
30 hydroxypropylcellulose, methylcellulose, hydroxypropyl methylcellulose acetate succinate or hydroxypropyl methylcellulose phthalate; film-forming acrylic polymers, for example methacrylate-methylmethacrylate copolymers; and film-forming vinyl polymers, for example polyvinyl alcohols or polyvinyl acetate phthalate. In some embodiments, the film-forming polymer is a water-soluble film-forming polymer, particularly a water-soluble cellulose ether
35 for example hydroxypropyl methylcellulose (particularly hydroxypropyl methylcellulose with a dynamic viscosity of from 2 to 18cP (measured in a 2%w/v solution at 20°C) and selected from, for example grades 1828, 2208, 2906 and especially 2910 as defined hereinbefore).

The amount of film-forming agent used will depend upon the desired properties of the film coating and the particular amount needed to achieve a desired property may be selected by those skilled in the art. Generally, the film forming agent will be present in an amount of from 40 to 90% by weight of the film coating, for example from 50 to 80% of the film coating. In
5 certain embodiments, the film-forming agent is typically present at from about 0.5 to 5% by weight of the formulation. In other embodiments, said film-forming agent is present at from about 2.5 to 5% by weight of the formulation.

Optionally the film coating contains additional components such as plasticizer, colorants,
10 dispersion aids and opacifiers. Plasticizers may be used to improve film flexibility and durability and adhesion properties of the film coating. Suitable plasticizers include, for example glycerin, acetylated monoglycerides, citrate esters (for example triethyl citrate), propylene glycols, polyethylene glycols (for example polyethylene glycols with a molecular weight of from 200 to 500, particularly 300), triacetin (glycerol tri-acetate), triglycerides (for
15 example castor oil), or phthalate esters (for example diethylphthalate). Generally, the plasticizer, when used, is present in an amount of from 1 to 20%, for example 5 to 15% by weight of the film coating.

Suitable opacifiers and colorants are well known and include for example titanium dioxide,
20 ferric oxides (for example iron oxide).

Suitable dispersion aids include, for example talc.

In some embodiments, the film coating comprises:
25 (i) from 50 to 100 (e.g., from 50 to 80 parts of a water-soluble cellulose ether (e.g., hydroxypropyl methylcellulose, particularly hydroxypropyl methylcellulose with a dynamic viscosity of from 2 to 18cP (measured in a 2%w/v solution at 20°C), for example grades 2910, 1828, 2208 or 2906 as defined hereinbefore with a dynamic viscosity of from 5 to 7cP);
30 (ii) from 0 to 25 (particularly from 5 to 20 parts) parts plasticiser (e.g., polyethylene glycol, e.g., polyethylene glycol with a molecular weight of from 200 to 500); and
(iii) from 0 to 50 (particularly from 0 to 30) parts in total of opacifiers (e.g., titanium dioxide), colorants (e.g., iron oxide) and dispersion aids; wherein all parts are by weight and the sum of the parts (i)+(ii)+(iii) = 100.

35

The coating may comprise, for example, 2.0 to 8.0 wt% of the composition, e.g., from about 3 to 6%, or from about 3.5 to 5.0 wt%.

Tablets

In one embodiment, the pharmaceutical tablet comprises 20mg AZD5305 as a free base.

- 5 In one embodiment, the pharmaceutical tablet comprises 40mg AZD5305 as a free base.

In one embodiment, the pharmaceutical tablet comprises 60mg AZD5305 as a free base.

Particular tablet embodiments are set out below:

Component	20mg tablet Quantity per unit (mg)	40mg tablet Quantity per unit (mg)	60mg tablet Quantity per unit (mg)
AZD5305	20.0	40.0	60.0
Microcrystalline cellulose	55.0	110.0	165.0
Calcium hydrogen phosphate anhydrous	18.5	37.5	55.5
Hydroxypropyl cellulose low substituted	5.0	10.0	15.0
Magnesium stearate	1.5	3.0	4.5
Tablet core weight	100.0	200.0	300.0
Nominal coated tablet weight	105.0 ^a	208.0 ^b	310.5 ^c

- 10 ^a Corresponding to approximately 5.0% of tablet core weight, to provide a coat thickness of approximately 0.05mg/mm².

^b Corresponding to approximately 4.0% of tablet core weight, to provide a coat thickness of approximately 0.05mg/mm²

- ^c Corresponding to approximately 3.5% of tablet core weight, to provide a coat thickness of approximately 0.05mg/mm²
- 15

Tablet manufacture

In some embodiments, the tablet is prepared by direct compression.

In some embodiments, the tablet is prepared by roller compaction.

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In some embodiments, the tablet is prepared by first dry blending the AZD5305, or pharmaceutical salt thereof, one or more disintegrants and the one or more diluents.

Following this the one or more lubricants can be added with or without roller compaction, before the tablet is made by compression.

Any coating is added following compression.

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Treatment

The language “treat,” “treating” and “treatment” includes the reduction or inhibition of enzyme or protein activity related to PARP-1 in a subject, amelioration of one or more symptoms of diseases or conditions in which inhibition of PARP1 is beneficial in a subject, or the slowing or delaying of progression of diseases or conditions in which inhibition of PARP1 is beneficial in a subject. The language “treat,” “treating” and “treatment” also includes the reduction or inhibition of the growth of a tumor or proliferation of cancerous cells in a subject.

15 The language “inhibit,” “inhibition” or “inhibiting” includes a decrease in the baseline activity of a biological activity or process.

The term “subject” includes warm-blooded mammals, for example, primates, dogs, cats, rabbits, rats, and mice. In some embodiments, the subject is a primate, for example, a human. In some embodiments, the subject is suffering from diseases or conditions in which inhibition of PARP1 is beneficial.

20 In some embodiments, AZD5305, or a pharmaceutically acceptable salt thereof, is administered in a dose of 10 to 140 mg per day of the free base. The daily dose may be up to 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg of the free base. The daily dose may be at least 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg or 130 mg of the free base.

30 In some embodiments, AZD5305, or a pharmaceutically acceptable salt thereof, is administered in a daily dose of 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg of the free base.

35 In some embodiments, AZD5305, or a pharmaceutically acceptable salt thereof, is administered once a day (QD). In some embodiments, AZD5305 is administered in a dose of 10 to 140 mg QD. The once daily dose may be up to 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg of the free base. The once daily dose may be at least 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg or 130 mg of the free base.

In some embodiments, AZD5305 is administered in a once daily dose (QD) of 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg of the free base.

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In some embodiments, the cancer treated may be deficient in Homologous Recombination (HR) dependent DNA DSB repair activity. The HR dependent DNA DSB repair pathway repairs double-strand breaks (DSBs) in DNA via homologous mechanisms to reform a continuous DNA helix (Khanna and Jackson 2001). The components of the HR dependent

10 DNA DSB repair pathway include, but are not limited to, ATM (NM_000051), RAD51 (NM_002875), RAD51L1 (NM_002877), RAD51C (NM_002876), RAD51L3 (NM_002878), DMC1 (NM_007068), XRCC2 (NM_005431), XRCC3 (NM_005432), RAD52 (NM_002879), RAD54L (NM_003579), RAD54B (NM_012415), BRCA1 (NM_007295), BRCA2 (NM_000059), RAD50 (NM_005732), MRE11A (NM_005590) and NBS1 (NM_002485).

15 Other proteins involved in the HR dependent DNA DSB repair pathway include regulatory factors such as EMSY (Hughes-Davies 2003). HR components are also described in Wood 2001.

A cancer which is deficient in HR dependent DNA DSB repair may comprise or consist of
20 one or more cancer cells which have a reduced or abrogated ability to repair DNA DSBs through that pathway, relative to normal cells i.e. the activity of the HR dependent DNA DSB repair pathway may be reduced or abolished in the one or more cancer cells.

The activity of one or more components of the HR dependent DNA DSB repair pathway may
25 be abolished in the one or more cancer cells of an individual having a cancer which is deficient in HR dependent DNA DSB repair. Components of the HR dependent DNA DSB repair pathway are well characterised in the art (see for example, Wood 2001) and include the components listed above.

30 In some embodiments, the cancer cells may have a BRCA1 and/or a BRCA2 deficient phenotype i.e. BRCA1 and/or BRCA2 activity is reduced or abolished in the cancer cells. Cancer cells with this phenotype may be deficient in BRCA1 and/or BRCA2, i.e. expression and/or activity of BRCA1 and/or BRCA2 may be reduced or abolished in the cancer cells, for example by means of mutation or polymorphism in the encoding nucleic acid, or by means of
35 amplification, mutation or polymorphism in a gene encoding a regulatory factor, for example the EMSY gene which encodes a BRCA2 regulatory factor (Hughes-Davies 2003).

BRCA1 and BRCA2 are known tumour suppressors whose wild-type alleles are frequently lost in tumours of heterozygous carriers (Jasin 2002; Tutt 2002). The association of BRCA1 and/or BRCA2 mutations with breast cancer is well-characterised in the art (Radice 2002). Amplification of the EMSY gene, which encodes a BRCA2 binding factor, is also known to be associated with breast and ovarian cancer. Carriers of mutations in BRCA1 and/or BRCA2 are also at elevated risk of certain cancers, including breast, ovary, pancreas, prostate, hematological, gastrointestinal and lung cancer.

In some embodiments, the individual is heterozygous for one or more variations, such as mutations and polymorphisms, in BRCA1 and/or BRCA2 or a regulator thereof. The detection of variation in BRCA1 and BRCA2 is well-known in the art and is described, for example in EP 699 754, EP 705 903, Neuhausen and Ostrander 1992; Chappuis and Foulkes 2002; Janatová 2003; Jancárková 2003). Determination of amplification of the BRCA2 binding factor EMSY is described in Hughes-Davies 2003.

Mutations and polymorphisms associated with cancer may be detected at the nucleic acid level by detecting the presence of a variant nucleic acid sequence or at the protein level by detecting the presence of a variant (i.e. a mutant or allelic variant) polypeptide.

In some embodiments, AZD5305, or a pharmaceutically acceptable salt thereof, is administered as a monotherapy.

In some embodiments, AZD5305, or a pharmaceutically acceptable salt thereof, is administered in combination with one or more other agents which can be used in treating diseases and conditions in which inhibition of PARP1 or PARP 1 function is of therapeutic significance.

Examples

The compounds of the application will now be further explained by reference to the following non-limiting examples.

Example 1

Tablets with the following composition were made using roller compaction:

Component	Function	Quantity (mg)
AZD5305	Active	20.0
Microcrystalline cellulose	Filler	55.0
Calcium hydrogen phosphate anhydrous	Filler	18.5
Hydroxypropyl cellulose low substituted	Disintegrant	5.0
Magnesium stearate	Lubricant	1.5
Tablet core weight		100.0

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Tablets were tested to confirm AZD5305 strength. A gradient reverse phase LC method was used with mobile phases consisting of ammonium hydroxide in water and ammonium hydroxide in acetonitrile, a USP L1 stationary phase and UV detection. The conditions were selective to AZD5305 in the presence of excipients, synthetic impurities and degradation products. Quantification was performed against an external AZD5305 reference standard, analysed using the same conditions on the same system. AZD5305 was measured to be within 95-105% of the assay target value. The amount of AZD5305 per tablet was found to be 20.06 mg, i.e. 100.3% of target strength.

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The dissolution of these tablets was measured in a standard test with greater than 80% dissolution occurring in 900 ml of pH1.2 media in a USP (United States Pharmacopoeia) apparatus 2 at 75rpm at 30 minutes.

Example 2

Tablets with the following composition were made using direct compression:

Component	Function	Quantity (mg)
AZD5305	Active	60.0
Microcrystalline cellulose	Filler	165.0
Calcium hydrogen phosphate anhydrous	Filler	55.5
Hydroxypropyl cellulose low substituted	Disintegrant	15.0
Magnesium stearate	Lubricant	4.5
Tablet core weight		300.0

- 5 Tablets were tested to confirm AZD5305 strength. A gradient reverse phase LC method was used with mobile phases consisting of ammonium hydroxide in water and ammonium hydroxide in acetonitrile, a USP L1 stationary phase and UV detection. The conditions were selective to AZD5305 in the presence of excipients, synthetic impurities and degradation products. Quantification was performed against an external AZD5305 reference standard,
- 10 analysed using the same conditions on the same system. AZD5305 was measured to be within 95-105% of the assay target value. The amount of AZD5305 per tablet was found to be 58.62 mg, i.e. 97.7% of target strength.

- The dissolution of these tablets was measured in a standard test with greater than 80% dissolution occurring in 900 ml of pH1.2 media in a USP (United States Pharmacopoeia) apparatus 2 at 75rpm at 30 minutes.
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References

- 20 A number of publications are cited above in order to more fully describe and disclose the invention and the state of the art to which the invention pertains. Full citations for these references are provided below. The entirety of each of these references is incorporated herein.

	Reference	Doi
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Hughes-Davies 2003	Hughes-Davies, et al., Cell, 115, 523-535 (2003)	10.1016/s0092-8674(03)00930-9
Janatová 2003	Janatová M, et al., Neoplasma, 50(4), 246-50 (2003)	PMID: 12937835
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Jasin 2002	Jasin M., Oncogene, 21(58), 8981-93 (2002)	10.1038/sj.onc.1206176
Johannes 2021	Johannes, JW, et al., <i>J Med Chem</i> 2021, 64, 14498-14512	10.1021/acs.jmedchem.1c01012
Khanna and Jackson 2001	Khanna KK and Jackson SP, Nat. Genet. 27(3): 247-254 (2001)	10.1038/85798
Neuhausen and Ostrander 1992	Neuhausen SL and Ostrander EA, <i>Genet. Test</i> , 1, 75-83 (1992)	10.1089/gte.1997.1.75
O'Connor 2015	O'Connor MJ, Mol Cell (2015) 60(4):547-560	10.1016/j.molcel.2015.10.040
Radice 2002	Radice, P.J., Exp Clin Cancer Res., 21(3 Suppl), 9-12 (2002)	PMID: 12585647
Tutt 2002	Tutt, et al., Trends Mol Med., 8(12), 571-576, (2002)	10.1016/s1471-4914(02)02434-6
Turner 2004	Turner N, et al., Nat Rev Cancer, 2004; 4: 814-819	10.1038/nrc1457
Wood 2001	Wood, et al., Science, 291, 1284-1289 (2001)	10.1126/science.1056154

Statements

1. A pharmaceutical composition comprising:
 - (a) from about 10.0 to about 25.0 wt% AZD5305;
 - 5 (b) from about 0.5 to about 8.0 wt% of one or more pharmaceutical disintegrants;
 - (c) from about 0.5 to about 2.5 wt% of one or more pharmaceutical lubricants;
 - (d) from about 64.5 to about 74.0 wt% of one or more pharmaceutical diluentswherein the component weights add up to 100, and wherein AZD5305 may be in the form of a pharmaceutically acceptable salt.
- 10 2. The pharmaceutical composition according to statement 1, comprising AZD5305 in an amount:
 - (i) from about 11.0 wt% to about 24.0 wt%;
 - (ii) from about 12.0 wt% to about 23.0 wt%;
 - 15 (iii) from about 13.0 wt% to about 22.0 wt%;
 - (iv) from about 14.0 wt% to about 21.0 wt%;
 - (v) of about 10.0 wt%, 15.0 wt%, 20.0 wt%, or 25.0 wt%,and wherein AZD5305 may be in the form of a pharmaceutically acceptable salt.
- 20 3. The pharmaceutical composition according to either statement 1 or statement 2, wherein the one or more pharmaceutical disintegrants is selected from alginic acid, calcium alginate, carboxymethylcellulose calcium, chitosan, croscarmellose sodium, crospovidone, glycine, guar gum, hydroxypropyl cellulose, low-substituted hydroxypropyl cellulose, magnesium aluminium silicate, methylcellulose, povidone, sodium alginate, sodium
25 carboxymethylcellulose, sodium starch glycolate and starch.
4. The pharmaceutical composition according to any statement 3, wherein the one or more pharmaceutical disintegrants is low-substituted hydroxypropyl cellulose.
- 30 5. The pharmaceutical composition according to any one of statements 1 to 4, comprising one or more pharmaceutical disintegrants in an amount:
 - (i) from about 1.0 wt% to about 7.0 wt%;
 - (ii) from about 3.0 wt% to about 6.0 wt%;
 - (iii) of about 1.0 wt%, 2.0 wt%, 3.0 wt%, 4.0 wt%, 5.0 wt%, 6.0 wt% or 7.0 wt%.
- 35 6. The pharmaceutical composition according to any one of statements 1 to 5, wherein the one or more pharmaceutical lubricants is selected from calcium stearate, glyceryl

behenate, glyceryl monostearate, glyceryl palmitostearate, a mixture of behenate esters of glycerine, leucine, magnesium stearate, myristic acid, palmitic acid, poloxamer, polyethylene glycol, potassium benzoate, sodium benzoate, sodium lauryl sulfate, sodium stearate, sodium stearyl fumarate, stearic acid, talc, tribehenin and zinc stearate.

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7. The pharmaceutical composition according to statement 6, wherein the one or more pharmaceutical lubricants comprises one or more pharmaceutical lubricants selected from calcium stearate, glyceryl behenate, glyceryl monostearate, glyceryl palmitostearate, a mixture of behenate esters of glycerine (e.g., a mixture of glyceryl behenate, tribehenin and glyceryl behenate), leucine, magnesium stearate, myristic acid, palmitic acid, poloxamer, polyethylene glycol, potassium benzoate, sodium benzoate, sodium lauryl sulfate, sodium stearate, stearic acid, talc, tribehenin and zinc stearate.

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8. The pharmaceutical composition according to statement 7, wherein the one or more pharmaceutical lubricants comprises glyceryl behenate, magnesium stearate, stearic acid, or a combination thereof.

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9. The pharmaceutical composition according to statement 8, wherein the one or more pharmaceutical lubricants is glyceryl behenate, magnesium stearate, or a combination thereof.

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10. The pharmaceutical composition according to statement 9, wherein the one or more pharmaceutical lubricants is magnesium stearate.

11. The pharmaceutical composition according to any one of statements 1 to 10, comprising one or more pharmaceutical lubricants in an amount:

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(i) from about 1.0 wt% to about 2.0 wt%;

(ii) from about 1.25 wt% to about 1.75 wt%;

(iii) of about 1.0 wt%, 1.25 wt%, 1.5 wt%, 1.75 wt% or 2.0 wt%.

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12. The pharmaceutical composition according to any one of statements 1 to 11, wherein the one or more pharmaceutical diluents selected from microcrystalline cellulose, calcium carbonate, calcium phosphate, calcium hydrogen phosphate, calcium sulfate, cellulose acetate, erythritol, ethylcellulose, fructose, inulin, isomalt, lactitol, lactose, magnesium carbonate, magnesium oxide, maltitol, maltodextrin, maltose, mannitol, polydextrose, polyethylene glycol, pullulan, simethicone, sodium bicarbonate, sodium carbonate, sodium chloride, sorbitol, starch, sucrose, trehalose and xylitol.

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13. The pharmaceutical composition according to any one of statements 1 to 12, wherein the one or more pharmaceutical diluents is microcrystalline cellulose.
- 5 14. The pharmaceutical composition according to any one of statements 1 to 12, which comprises two or more pharmaceutical diluents.
15. The pharmaceutical composition according to statement 14, wherein the two pharmaceutical diluents are microcrystalline cellulose and calcium hydrogen phosphate.
- 10 16. The pharmaceutical composition according to statement 14, comprising 55.0 wt% microcrystalline cellulose and 18.5 wt% calcium hydrogen phosphate.
17. The pharmaceutical composition according to any one of statements 1 to 15, comprising one or more pharmaceutical diluents in an amount:
- 15 (i) from about 66.0 wt% to about 74.0 wt%;
- (ii) from about 68.0 wt% to about 74.0 wt%;
- (iii) from about 70.0 wt% to about 74.0 wt%;
- (iv) from about 66.0 wt% to about 70.0 wt%;
- 20 (v) of about 64.5 wt%, 65.0 wt%, 66.0 wt%, 67.0 wt%, 68.0 wt%, 69.0 wt%, 70.0 wt%, 71.0 wt%, 72.0 wt%, 73.0 wt%, or 74.0 wt%.
18. A pharmaceutical tablet comprising the pharmaceutical composition of any one of statements 1 to 17.
- 25 19. The pharmaceutical tablet according to statement 18, wherein the pharmaceutical tablet comprises a tablet core which comprises the pharmaceutical composition, and the tablet core has a coating.
- 30 20. A method of treatment or prophylaxis of diseases or conditions in which inhibition of PARP1 is beneficial, comprising administering to the subject AZD5305, or a pharmaceutically acceptable salt thereof, in the form of a pharmaceutical composition according to any one of statements 1 to 17 or a pharmaceutical tablet according to either statement 18 or statement 19.
- 35 21. The method according to statement 20, wherein the disease or condition in which inhibition of PARP1 is beneficial is cancer.

22. The method according to statement 21, wherein the cancer is breast, ovary, pancreas, prostate, hematological, gastrointestinal such as gastric and colorectal, or lung cancer.

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23. The method according to any one of statements 20 to 22, wherein AZD5305 is administered in a dose of 10mg to 140 mg per day, and wherein AZD5305 may be in the form of a pharmaceutically acceptable salt.

10 24. The method according to statement 23, wherein AZD5305 is administered in a dose of up to 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg per day, and wherein AZD5305 may be in the form of a pharmaceutically acceptable salt.

15 25. The method according to either statement 23 or statement 24, wherein AZD5305 is administered in a dose of at least 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg or 130 mg per day, and wherein AZD5305 may be in the form of a pharmaceutically acceptable salt.

20 26. The method according to statement 23, wherein AZD5305 is administered in a dose of 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg per day, and wherein AZD5305 may be in the form of a pharmaceutically acceptable salt.

25 27. The method according to any one of statements 20 to 26, wherein AZD5305, or a pharmaceutically acceptable salt thereof, is administered once daily.

28. AZD5305, or a pharmaceutically acceptable salt thereof, for use in the treatment or prophylaxis of diseases or conditions in which inhibition of PARP1 is beneficial in a subject,
30 wherein said AZD5305 or pharmaceutically acceptable salt thereof is administered in the form of a pharmaceutical composition according to any one of statements 1 to 17 or a pharmaceutical tablet according to either statement 18 or statement 19.

29. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to
35 statement 28, wherein the disease or condition in which inhibition of PARP1 is beneficial is cancer.

30. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to statement 29, wherein the cancer is breast, ovary, pancreas, prostate, hematological, gastrointestinal such as gastric and colorectal, or lung cancer.
- 5 31. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to any one of statements 28 to 30, wherein AZD5305 is administered in a dose of 10mg to 140 mg per day.
- 10 32. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to statement 31, wherein AZD5305 is administered in a dose of up to 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg per day.
- 15 33. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to either statement 30 or statement 31, wherein AZD5305 is administered in a dose of at least 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg or 130 mg per day.
- 20 34. AZD5305, or a pharmaceutically acceptable salt thereof, for use according statement 31, wherein AZD5305 is administered in a dose of 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg per day.
35. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to any one of statements 28 to 34, wherein AZD5305 is administered once daily.
- 25 36. The use of AZD5305, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in the treatment of or prophylaxis of diseases or conditions in which inhibition of PARP1 is beneficial, wherein said AZD5305 is administered in the form of a pharmaceutical composition according to any one of statements 1 to 17 or a pharmaceutical tablet according to either statement 18 or statement 19.
- 30 37. The use of AZD5305, or a pharmaceutically acceptable salt thereof, according to statement 36, wherein the disease or condition in which inhibition of PARP1 is beneficial is cancer.
- 35 38. The use of AZD5305, or a pharmaceutically acceptable salt thereof, according to statement 37, wherein the cancer is breast, ovary, pancreas, prostate, hematological, gastrointestinal such as gastric and colorectal, or lung cancer.

39. The use of AZD5305, or a pharmaceutically acceptable salt thereof, according to any one of statements 36 to 38, wherein said treatment administering to the subject AZD5305 in a daily dose of 10 to 140 mg.

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40. The use of AZD5305, or a pharmaceutically acceptable salt thereof, according to statement 39, wherein AZD5305 is administered in a dose of up to 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg per day.

10 41. The use of AZD5305, or a pharmaceutically acceptable salt thereof, according to either statement 39 or statement 40, wherein AZD5305 is administered in a dose of at least 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg or 130 mg per day.

15 42. The use of AZD5305, or a pharmaceutically acceptable salt thereof, according to statement 39, wherein AZD5305 is administered in a dose of 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg per day.

20 43. The use of AZD5305, or a pharmaceutically acceptable salt thereof, according to any one of statements 36 to 42, wherein AZD5305 is administered once daily.

Claims

1. A pharmaceutical composition comprising:
 - (a) from about 10.0 to about 25.0 wt% 5-{4-[(7-ethyl-6-oxo-5,6-dihydro-1,5-naphthyridin-3-yl)methyl]piperazin-1-yl}-N-methylpyridine-2-carboxamide ("AZD5305");
 - (b) from about 0.5 to about 8.0 wt% of one or more pharmaceutical disintegrants;
 - (c) from about 0.5 to about 2.5 wt% of one or more pharmaceutical lubricants; and
 - (d) from about 64.5 to about 74.0 wt% of one or more pharmaceutical diluentswherein the component weights add up to 100, and wherein AZD5305 may be in the form of a pharmaceutically acceptable salt.
2. The pharmaceutical composition according to claim 1, comprising AZD5305 in an amount:
 - (i) from about 11.0 wt% to about 24.0 wt%;
 - (ii) from about 12.0 wt% to about 23.0 wt%;
 - (iii) from about 13.0 wt% to about 22.0 wt%;
 - (iv) from about 14.0 wt% to about 21.0 wt%; or
 - (v) of about 10.0 wt%, 15.0 wt%, 20.0 wt%, or 25.0 wt%,and wherein AZD5305 may be in the form of a pharmaceutically acceptable salt.
3. The pharmaceutical composition according to either claim 1 or claim 2, wherein the one or more pharmaceutical disintegrants is low-substituted hydroxypropyl cellulose.
4. The pharmaceutical composition according to any one of claims 1 to 3, comprising one or more pharmaceutical disintegrants in an amount:
 - (i) from about 1.0 wt% to about 7.0 wt%;
 - (ii) from about 3.0 wt% to about 6.0 wt%; or
 - (iii) of about 1.0 wt%, 2.0 wt%, 3.0 wt%, 4.0 wt%, 5.0 wt%, 6.0 wt% or 7.0 wt%.
5. The pharmaceutical composition according to any one of claims 1 to 4, wherein the one or more pharmaceutical lubricants comprises glyceryl behenate, magnesium stearate, stearic acid, or a combination thereof.
6. The pharmaceutical composition according to claim 5, wherein the one or more pharmaceutical lubricants is magnesium stearate.

7. The pharmaceutical composition according to any one of claims 1 to 6, comprising one or more pharmaceutical lubricants in an amount:
- (i) from about 1.0 wt% to about 2.0 wt%;
 - (ii) from about 1.25 wt% to about 1.75 wt%; or
- 5 (iii) of about 1.0 wt%, 1.25 wt%, 1.5 wt%, 1.75 wt% or 2.0 wt%.
8. The pharmaceutical composition according to any one of claims 1 to 7, wherein the one or more pharmaceutical diluents is microcrystalline cellulose.
- 10 9. The pharmaceutical composition according to any one of claims 1 to 7, which comprises two or more pharmaceutical diluents.
10. The pharmaceutical composition according to claim 9, wherein the two pharmaceutical diluents are microcrystalline cellulose and calcium hydrogen phosphate.
- 15 11. The pharmaceutical composition according to any one of claims 1 to 10, comprising one or more pharmaceutical diluents in an amount:
- (i) from about 66.0 wt% to about 74.0 wt%;
 - (ii) from about 68.0 wt% to about 74.0 wt%;
- 20 (iii) from about 70.0 wt% to about 74.0 wt%;
- (iv) from about 66.0 wt% to about 70.0 wt%; or
 - (v) of about 64.5 wt%, 65.0 wt%, 66.0 wt%, 67.0 wt%, 68.0 wt%, 69.0 wt%, 70.0 wt%, 71.0 wt%, 72.0 wt%, 73.0 wt%, or 74.0 wt%.
- 25 12. A pharmaceutical tablet comprising the pharmaceutical composition of any one of claims 1 to 11.
13. The pharmaceutical tablet according to claim 12, wherein the pharmaceutical tablet comprises a tablet core which comprises the pharmaceutical composition, and the tablet
- 30 core has a coating.
14. 5-{4-[(7-ethyl-6-oxo-5,6-dihydro-1,5-naphthyridin-3-yl)methyl]piperazin-1-yl}-N-methylpyridine-2-carboxamide ("AZD5305"), or a pharmaceutically acceptable salt thereof, for use in the treatment or prophylaxis of diseases or conditions in which inhibition of
- 35 PARP1 is beneficial in a subject, wherein said AZD5305 or pharmaceutically acceptable salt thereof is administered in the form of a pharmaceutical composition according to any one of claims 1 to 11 or a pharmaceutical tablet according to either claim 12 or claim 13.

15. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to claim 14, wherein the disease or condition in which inhibition of PARP1 is beneficial is cancer.

5 16. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to claim 15, wherein the cancer is breast, ovary, pancreas, prostate, hematological, gastrointestinal such as gastric and colorectal, or lung cancer.

10 17. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to any one of claims 14 to 16, wherein AZD5305 is administered in a dose of 10 mg to 140 mg per day.

15 18. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to claim 17, wherein AZD5305 is administered in a dose of up to 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg per day, and wherein AZD5305 is administered in a dose of at least 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg or 130 mg per day.

20 19. AZD5305, or a pharmaceutically acceptable salt thereof, for use according claim 17, wherein AZD5305 is administered in a dose of 10 mg, 20 mg, 30 mg, 40mg, 50 mg, 60 mg, 70 mg, 80 mg, 90 mg, 100 mg, 110 mg, 120 mg, 130 mg or 140 mg per day.

25 20. AZD5305, or a pharmaceutically acceptable salt thereof, for use according to any one of claims 14 to 19, wherein AZD5305 is administered once daily.