Claims

1. 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride solvate excluding 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride monohydrate crystalline modification H2:

   Form H2:

Peak No.	d/Å	°2θ (Cu-Kα_1 radiation)	(h, k, l)
1	8.71	10.1	(1, 0, 0)
2	8.22	10.8	(-1, 1, 1)
3	7.59	11.6	(1, 2, 0)
4	6.78	13.0	(0, 3, 1)
5	6.58	13.5	(-1, 3, 1)
6	5.73	15.4	(-1, 4, 1)
7	4.98	17.8	(-1, 1, 2)
8	4.84	18.3	(-2, 1, 1)
9	4.68	19.0	(-2, 2, 1)
10	4.43	20.0	(-2, 3, 1)
11	4.35	20.4	(2, 0, 0)
12	3.73	23.9	(-2, 4, 2)
13	3.64	24.5	(0, 5, 2)
14	3.39	26.3	(0, 6, 2)
15	3.13	28.5	(-3, 2, 2)

2. The compound of claim 1 in its crystalline modifications.

3. 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride anhydrate.

4. The compound of claim 3 in its crystalline modification A1, which is characterized by XRD peaks comprising 4,4°, 15.9° and 22,7° (in °2θ using Cu-Kα_1 radiation, ± 0.1°).

5. The compound according to any of claims 3 to 4, which is characterized by the following XRD data:
Form A1:

Peak No.	**d/Å**	**°2θ (Cu-Kα_1 radiation) ± 0.1°**
1	20.08	4.4
2	8.55	10.3
3	7.43	11.9
4	5.70	15.5
5	5.56	15.9
6	4.99	17.8
7	4.86	18.2
8	4.74	18.7
9	4.55	19.5
10	4.46	19.9
11	4.27	20.8
12	4.10	21.6
13	3.91	22.7
14	3.82	23.3
15	3.65	24.3

6. 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride hydrate excluding 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-

dihydro-pyridazin-3-yl)-benzonitrile hydrochloride monohydrate crystalline modification H2 according to claim 1:

Form H2:

Peak No.	**d/Å**	**°2θ (Cu-Kα_1 radiation)**	**(h, k, l)**
1	8.71	10.1	(1, 0, 0)
2	8.22	10.8	(-1, 1, 1)
3	7.59	11.6	(1, 2, 0)
4	6.78	13.0	(0, 3, 1)
5	6.58	13.5	(-1, 3, 1)
6	5.73	15.4	(-1, 4, 1)
7	4.98	17.8	(-1, 1, 2)
8	4.84	18.3	(-2, 1, 1)
9	4.68	19.0	(-2, 2, 1)
10	4.43	20.0	(-2, 3, 1)
11	4.35	20.4	(2, 0, 0)
12	3.73	23.9	(-2, 4, 2)
13	3.64	24.5	(0, 5, 2)
14	3.39	26.3	(0, 6, 2)
15	3.13	28.5	(-3, 2, 2)

7. The compound of claim 3 in its crystalline modification NF6, which is characterized by XRD peaks comprising 16,8°, 18.2° and 25,8° (in °2θ using Cu-Kα_1 radiation, ± 0.1°).

8 The compound according to any of claims 3, 7, which is characterized by the following XRD data:

Form NF6:

Peak No.	**d/Å**	**°2θ (Cu-Kα_1 radiation) ± 0.1°**
1	17.66	5.0
2	11.07	8.0
3	10.53	8.4
4	9.35	9.4
5	8.77	10.1
6	6.55	13.5
7	5.83	15.2
8	5.26	16.8
9	4.88	18.2
10	4.54	19.5
11	4.48	19.8
12	4.38	20.3
13	4.06	21.9
14	3.66	24.3
15	3.50	25.4
16	3.45	25.8
17	3.32	26.8
18	3.27	27.2
19	3.21	27.8
20	3.12	28.6

9. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound according to any of claims 1 to 8.

10. The pharmaceutical composition as claimed in claim 9 further comprising at least one additional compound selected from the group consisting of physiologically acceptable excipients, auxiliaries, adjuvants, diluents, carriers and/or additional pharmaceutically active substances other than the compounds according to any of claims 1 to 8.

11. Medicament comprising at least one compound according to any of claims 1 to 8 or a pharmaceutical composition according to any of claims 9 to 10.

12. Use of at least one compound according to any of claims 1 to 8 or a pharmaceutical composition according to any of claims 9 to 10 in the manufacture of a medicament for the treatment and/or prophylaxis of physiological and/or pathophysiological conditions, which are caused, mediated and/or propagated by the inhibition, regulation and/or modulation of signal transduction of kinases, in particular by the inhibition of tyrosine kinases, preferably Met-kinase, and wherein the treatment and/or prophylaxis of physiological and/or pathophysiological conditions are selected from the group consisting of: “cancer, tumour, malignant tumours, benign tumours, solid tumours, sarcomas, carcinomas, hyperproliferative disorders, carcinoids, Ewing sarcomas, Kaposi sarcomas, brain tumours, tumours originating from the brain and/or the nervous system and/or the meninges, gliomas, glioblastomas, neuroblastomas, stomach cancer, kidney cancer, kidney cell carcinomas, prostate cancer, prostate carcinomas, connective tissue tumours, soft tissue sarcomas, pancreas tumours, liver tumours, head tumours, neck tumours, laryngeal cancer, oesophageal cancer, thyroid cancer, osteosarcomas, retinoblastomas, thymoma, testicular cancer, lung cancer, lung adenocarcinoma, small cell lung carcinoma, bronchial carcinomas, breast cancer, mamma carcinomas, intestinal cancer, colorectal tumours, colon carcinomas, rectum carcinomas, gynaecological tumours,

ovary tumours/ovarian tumours, uterine cancer, cervical cancer, cervix carcinomas, cancer of body of uterus, corpus carcinomas, endometrial carcinomas, urinary bladder cancer, urogenital tract cancer, bladder cancer, skin cancer, epithelial tumours, squamous epithelial carcinoma, basaliomas, spinaliomas, melanomas, intraocular melanomas, leukaemias, monocyte leukaemia, chronic leukaemias, chronic myelotic leukaemia, chronic lymphatic leukemia, acute leukaemias, acute myelotic leukaemia, acute lymphatic leukaemia and/or lymphomas".

13. The medicament as claimed in any of claims 11 to 12, wherein in such medicament comprises at least one additional pharmacologically active substance.

14. The medicament as claimed in any of claims 11 to 12, wherein the medicament is applied before and/or during and/or after treatment with at least one additional pharmacologically active substance.

15. Kit comprising a therapeutically effective amount of at least one compound according to any of claims 1 to 8 and/or at least one pharmaceutical composition as claimed in any of claims 9 to 10 and a therapeutically effective amount of at least one further pharmacologically active substance other than the compounds as claimed in any of claims 1 to 8.

16. Process for manufacturing crystalline modification A1 according to any of claims 4 to 5 comprising the steps:
    (a) dispersing 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile (free base) or one or more salts thereof in a solvent or a solvent mixture, preferably 2-propanole, optionally under stirring,
    (b) converting 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile (free base) or one

or more salts thereof into the corresponding hydrochloride salt by addition of etheric hydrochloric acid solution, optionally under stirring,

(c) heating up the resulting dispersion or solution of step (b) to elevated temperature T1, preferably 30° C to 95° C, more preferably 50° C, optionally under stirring, stirring until crystallization begins and continuing stirring at room temperature until completion of the crystallization process,

(d) isolating precipitated 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride anhydrate by solid-liquid separation, preferably filtration, optionally subsequent washing with a solvent or a solvent mixture, preferably ether, and optionally subsequent drying, preferably in vacuo, optionally at elevated temperature T2, preferably 30° C to 95° C, more preferably 70° C.

17. Process for manufacturing crystalline modification H2 of 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride monohydrate

Form H2:

Peak No.	**d/Å**	**°2θ (Cu-Kα_1 radiation)**	**(h, k, l)**
1	8.71	10.1	(1, 0, 0)
2	8.22	10.8	(-1, 1, 1)
3	7.59	11.6	(1, 2, 0)
4	6.78	13.0	(0, 3, 1)
5	6.58	13.5	(-1, 3, 1)
6	5.73	15.4	(-1, 4, 1)
7	4.98	17.8	(-1, 1, 2)
8	4.84	18.3	(-2, 1, 1)
9	4.68	19.0	(-2, 2, 1)

10	4.43	20.0	(-2, 3, 1)
11	4.35	20.4	(2, 0, 0)
12	3.73	23.9	(-2, 4, 2)
13	3.64	24.5	(0, 5, 2)
14	3.39	26.3	(0, 6, 2)
15	3.13	28.5	(-3, 2, 2)

comprising the steps:

(a) dispersing 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile (free base) or one or more salts thereof in a solvent or a solvent mixture, preferably acetone, optionally under stirring, and optionally heating up the resulting dispersion to elevated temperature T1, preferably 30° C to 95° C, more preferably 60° C, optionally under stirring,

(b) converting 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile (free base) or one or more salts thereof into the corresponding hydrochloride salt by addition of aqueous hydrochloric acid solution, optionally under stirring, heating up the resulting dispersion to elevated temperature T2, preferably 30° C to 95° C, more preferably 60° C, for one or more minutes or hours, preferably 30 min, optionally under stirring, and optionally adding further solvent or solvent mixture, preferably water, optionally under stirring,

(c) cooling down the dispersion of step (b) to room temperature, optionally under stirring, and incubating it at room temperature for one or more hours or days, optionally under stirring,

(d) isolating precipitated 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride monohydrate by solid-liquid separation, preferably filtration, optionally washing with a solvent or a solvent mixture, preferably acetone or THF, and optionally subsequent drying, preferably in vacuo, op-

tionally at elevated temperature T3, preferably 30° C to 95° C, more preferably 50° C.

18. Process for manufacturing crystalline modification H2 of 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride monohydrate
Form H2:

Peak No.	**d/Å**	**°2θ (Cu-Kα_1 radiation)**	**(h, k, l)**
1	8.71	10.1	(1, 0, 0)
2	8.22	10.8	(-1, 1, 1)
3	7.59	11.6	(1, 2, 0)
4	6.78	13.0	(0, 3, 1)
5	6.58	13.5	(-1, 3, 1)
6	5.73	15.4	(-1, 4, 1)
7	4.98	17.8	(-1, 1, 2)
8	4.84	18.3	(-2, 1, 1)
9	4.68	19.0	(-2, 2, 1)
10	4.43	20.0	(-2, 3, 1)
11	4.35	20.4	(2, 0, 0)
12	3.73	23.9	(-2, 4, 2)
13	3.64	24.5	(0, 5, 2)
14	3.39	26.3	(0, 6, 2)
15	3.13	28.5	(-3, 2, 2)

comprising the steps:

(a) dispersing 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile (free base) or one or more salts thereof in a solvent or a solvent mixture, preferably water, optionally under stirring,

(b) converting 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile (free base) or one or more salts thereof into the corresponding hydrochloride salt by addition of aqueous hydrochloric acid solution, optionally under stirring, heating up the resulting dispersion to elevated temperature T1, preferably 30° C to 100° C, more preferably 80° C to 100° C, optionally under stirring, and optionally solid-liquid separating, preferably filtrating it to obtain a solution,

(c) heating up again the resulting filtrate of step (b) to elevated temperature T2, preferably 30° C to 100° C, more preferably 78° C to 85° C, optionally under stirring, and subsequently cooling it down, preferably to 0° C to 40° C, more preferably to 0° C to 27° C, over one or more hours or days, optionally under stirring, and optionally cooling it further down, preferably to 0° C to 25° C, more preferably to 20° C, optionally under stirring,

(d) isolating precipitated 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride monohydrate by solid-liquid separation, preferably filtration, optionally washing with a solvent or a solvent mixture, preferably water, THF or acetone, and optionally subsequent drying, preferably in vacuo, optionally at elevated temperature T3, preferably 30° C to 95° C, more preferably 50° C to 55° C.

19. Process according to any of claims 17 to 18, wherein in step (b) 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile (free base) or one or more salts thereof is converted into the corresponding hydrochloride salt by addition of one or more chloride salts selected from the group consisting of: “alkaline metal chloride salt, alkaline earth metal chloride salt, ammonium chloride salt, quaternary organic ammonia chloride salt, transition metal chloride salt”.

20. Process for manufacturing crystalline modification H2 of 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride monohydrate

Form H2:

Peak No.	**d/Å**	**°2θ (Cu-Kα_1 radiation)**	**(h, k, l)**
1	8.71	10.1	(1, 0, 0)
2	8.22	10.8	(-1, 1, 1)
3	7.59	11.6	(1, 2, 0)
4	6.78	13.0	(0, 3, 1)
5	6.58	13.5	(-1, 3, 1)
6	5.73	15.4	(-1, 4, 1)
7	4.98	17.8	(-1, 1, 2)
8	4.84	18.3	(-2, 1, 1)
9	4.68	19.0	(-2, 2, 1)
10	4.43	20.0	(-2, 3, 1)
11	4.35	20.4	(2, 0, 0)
12	3.73	23.9	(-2, 4, 2)
13	3.64	24.5	(0, 5, 2)
14	3.39	26.3	(0, 6, 2)
15	3.13	28.5	(-3, 2, 2)

comprising the steps:

(a) re-crystallizing 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride monohydrate from a solvent or a solvent mixture, optionally under stirring.

21. Process for manufacturing crystalline modification NF6 according to any of claims 7 to 8 comprising the steps:

(a) dispersing 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile (free base) or one or more salts thereof in a solvent or a solvent mixture, preferably acetone, optionally under stirring,

(b) converting 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile (free base) or one or more salts thereof into the corresponding hydrochloride salt by addition of aqueous hydrochloric acid solution, optionally under stirring,

(c) isolating precipitated 3-(1-{3-[5-(1-methyl-piperidin-4-ylmethoxy)-pyrimidin-2-yl]-benzyl}-6-oxo-1,6-dihydro-pyridazin-3-yl)-benzonitrile hydrochloride anhydrate by solid-liquid separation, preferably filtration, optionally subsequent washing with a solvent or a solvent mixture, and optionally subsequent drying, preferably in vacuo, optionally at elevated temperature T2, preferably 30° C to 95° C, more preferably 65° C.