In one aspect, described herein is use of erdafitinib ~~an FGFR inhibitor~~ in the manufacture of a medicament for the treatment of urothelial carcinoma, wherein said treatment comprises: (a) a biological sample from a patient is to be evaluated for the presence of at least two FGFR genetic alterations, wherein: ~~(i) two or more of the at least two FGFR genetic alterations are FGFR2 fusions; (ii) one or more of the at least two FGFR genetic alterations is an FGFR2 fusion and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion;~~ (~~iii~~i) two or more of the at least two FGFR genetic alterations are FGFR3 mutations; (~~iv~~ii) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR2 fusion; or (iii~~v~~) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion; and (b) the patient is to be administered erdafitinib ~~an FGFR inhibitor~~ if the at least two FGFR genetic alterations are present in the sample; wherein erdafitinib is to be administered at a dose of 8 mg, in particular 8 mg once daily, with an option to uptitrate to 9 mg depending on serum phosphate levels (e.g. serum phosphate levels are < 5.5 mg/dL, or are < 7 mg/dL or range from and include 7 mg/dL to ≤9 mg/dL or are ≤9 mg/dL), and depending on treatment-related adverse events observed.

Also described herein are methods of treating urothelial carcinoma in a patient harboring at least two FGFR genetic alterations comprising, consisting of, or consisting essentially of administering a FGFR inhibitor to the patient, wherein: (a) two or more of the at least two FGFR genetic alterations are FGFR2 fusions; (b) one or more of the at least two FGFR genetic alterations is an FGFR2 fusion and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion; (c) two or more of the at least two FGFR genetic alterations are FGFR3 mutations; (d) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR2 fusion; or (e) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion.

In another aspect, described herein is use of erdafitinib ~~an FGFR inhibitor~~ in the manufacture of a medicament for the treatment of urothelial carcinoma in a patient harboring at least two FGFR genetic alterations, wherein ~~said FGFR inhibitor is to be administered to the patient when~~: ~~(a) two or more of the at least two FGFR genetic alterations are FGFR2 fusions; (b) one or more of the at least two FGFR genetic alterations is an FGFR2 fusion and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion; (c) two or more of the at least two FGFR genetic alterations are FGFR3 mutations;~~ (~~d~~a) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR2 fusion; or (~~e~~b) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion; and wherein erdafitinib is to be administered at a dose of 8 mg, in particular 8 mg once daily, with an option to uptitrate to 9 mg depending on serum phosphate levels (e.g. serum phosphate levels are < 5.5 mg/dL, or are < 7 mg/dL or range from and include 7 mg/dL to ≤9 mg/dL or are ≤9 mg/dL), and depending on treatment-related adverse events observed.

In certain examples, the methods of treating urothelial carcinoma in a patient harboring at least two FGFR genetic alterations further comprise evaluating a biological sample from the patient for the presence of the at least two FGFR genetic alterations prior to administration of the FGFR inhibitor.

In certain examples of the methods of treating urothelial carcinoma disclosed herein, two or more of the at least two FGFR genetic alterations are FGFR2 fusions. In some examples, two or more FGFR genetic alterations comprise FGFR2-BICC1 and FGFR2-CASP7.

In certain examples of the methods of treating urothelial carcinoma disclosed herein, one or more of the at least two FGFR genetic alterations is an FGFR2 fusion and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion. In some

examples, two or more FGFR genetic alterations comprise FGFR2-CASP7 and FGFR3-BAIAP2L1; FGFR2-CASP7 and FGFR3-TACC3 V1; or FGFR2-CASP7 and FGFR3-TACC3 V3.

In certain examples of the methods of treating urothelial carcinoma disclosed herein, two or more of the at least two FGFR genetic alterations are FGFR3 mutations. In some embodiments, two or more FGFR genetic alterations comprise FGFR3 G370C and FGFR3 S249C; FGFR3 R248C and FGFR3 Y373C; or FGFR3 S249C and FGFR3 Y373C.

In certain examples of the methods of treating urothelial carcinoma disclosed herein, one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR2 fusion. In some examples, two or more FGFR genetic alterations comprise FGFR3 G370C/FGFR2-BICC1; or FGFR3 S249C, FGFR3 Y373C, FGFR2-CASP7, FGFR3-BAIAP2L1, FGFR3-TACC3 V1 and FGFR3_TACC3 V3.

In certain examples of the methods of treating urothelial carcinoma disclosed herein, one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion. In some

What is claimed:

1. Use of erdafitinib ~~an FGFR inhibitor~~ in the manufacture of a medicament for the treatment of urothelial carcinoma, wherein said treatment comprises:

(a) a biological sample from a patient is to be evaluated for the presence of at least two FGFR genetic alterations, wherein:

~~(i) two or more of the at least two FGFR genetic alterations are FGFR2 fusions;~~

~~(ii) one or more of the at least two FGFR genetic alterations is an FGFR2 fusion and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion;~~

(~~iii~~i) two or more of the at least two FGFR genetic alterations are FGFR3 mutations;

(~~iv~~ii) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR2 fusion; or

(~~v~~iii) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion; and

(b) the patient is to be administered erdafitinib ~~an FGFR inhibitor~~ if the at least two FGFR genetic alterations are present in the sample;

wherein erdafitinib is to be administered at a dose of 8 mg, in particular 8 mg once daily, with an option to uptitrate to 9 mg depending on serum phosphate levels (e.g. serum phosphate levels are < 5.5 mg/dL, or are < 7 mg/dL or range from and include 7 mg/dL to ≤9 mg/dL or are ≤9 mg/dL), and depending on treatment-related adverse events observed.

2. Use of erdafitinib ~~an FGFR inhibitor~~ in the manufacture of a medicament for the treatment of urothelial carcinoma in a patient harboring at least two FGFR genetic alterations, wherein ~~said FGFR inhibitor is to be administered to the patient when~~:

~~(a) two or more of the at least two FGFR genetic alterations are FGFR2 fusions;~~

~~(b) one or more of the at least two FGFR genetic alterations is an FGFR2 fusion and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion;~~

~~(c) two or more of the at least two FGFR genetic alterations are FGFR3 mutations;~~

(~~d~~a) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR2 fusion; or

(~~e~~b) one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion;
and wherein erdafitinib is to be administered at a dose of 8 mg, in particular 8 mg once daily, with an option to uptitrate to 9 mg depending on serum phosphate levels (e.g. serum phosphate levels are < 5.5 mg/dL, or are < 7 mg/dL or range from and include 7 mg/dL to ≤9 mg/dL or are ≤9 mg/dL), and depending on treatment-related adverse events observed.

3. Use of erdafitinib ~~an FGFR inhibitor~~ according to claim 1 or 2 wherein the at least two FGFR genetic alterations comprise FGFR3 G370C and FGFR3 S249C; or FGFR3 R248C and FGFR3 Y373C.

4. Use of erdafitinib ~~an FGFR inhibitor~~ according to claim 1 or 2 wherein the at least two FGFR genetic alterations comprise FGFR3 G370C and FGFR2-BICC1; FGFR3 G370C and FGFR3-TACC3 V1; FGFR3 R248C and FGFR3-TACC3 V1; or FGFR3 R248C, FGFR3 S249 and FGFR3-TACC3 V1.

5. Use of erdafitinib ~~an FGFR inhibitor~~ according to claim 2, wherein a biological sample that had been obtained from the patient is to be evaluated for the presence of the at least two FGFR genetic alterations prior to administration of the FGFR inhibitor.

~~6. Use of an FGFR inhibitor according to claim 1 or 2, wherein two or more of the at least two FGFR genetic alterations are FGFR2 fusions.~~

~~7. Use of an FGFR inhibitor according to claim 6, wherein the two or more FGFR genetic alterations comprise FGFR2-BICC1 and FGFR2-CASP7.~~

~~8. Use of an FGFR inhibitor according to claim 1 or 2, wherein one or more of the at least two FGFR genetic alterations is an FGFR2 fusion and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion.~~

~~9. Use of an FGFR inhibitor according to claim 8, wherein the two or more FGFR genetic alterations comprise FGFR2-CASP7 and FGFR3-BAIAP2L1; FGFR2-CASP7 and FGFR3-TACC3 V1; or FGFR2-CASP7 and FGFR3-TACC3 V3.~~

~~10. Use of an FGFR inhibitor according to claim 1 or 2, wherein two or more of the at least two FGFR genetic alterations are FGFR3 mutations.~~

~~11. Use of an FGFR inhibitor according to claim 10, wherein the two or more FGFR genetic alterations comprise FGFR3 G370C and FGFR3 S249C; FGFR3 R248C and FGFR3 Y373C; or FGFR3 S249C and FGFR3 Y373C.~~

~~12.~~6. Use of erdafitinib ~~an FGFR inhibitor~~ according to claim 1 or 2, wherein one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR2 fusion.

~~13.~~7. Use of erdafitinib ~~an FGFR inhibitor~~ according to claim ~~12~~6, wherein the two or more FGFR genetic alterations comprise FGFR3 G370C/FGFR2-BICC1; or FGFR3 S249C, FGFR3 Y373C, FGFR2-CASP7, FGFR3-BAIAP2L1, FGFR3-TACC3 V1 and FGFR3-TACC3 V3.

~~14.~~8. Use of erdafitinib ~~an FGFR inhibitor~~ according to claim 1 or 2, wherein one or more of the at least two FGFR genetic alterations is an FGFR3 mutation and one or more of the at least two FGFR genetic alterations is an FGFR3 fusion.

~~15.~~9. Use of erdafitinib ~~an FGFR inhibitor~~ according to claim ~~14~~8, wherein the two or more FGFR genetic alterations comprise FGFR3 G370C and FGFR3-TACC3 V1; FGFR3 R248C and FGFR3-TACC3 V1; FGFR3 S249C and FGFR3-BAIAP2L1; FGFR3 R248C, FGFR3 S249 and FGFR3-TACC3 V1; or FGFR3 S249C, FGFR3 Y373C, FGFR2-CASP7, FGFR3-BAIAP2L1, FGFR3-TACC3 V1 and FGFR3-TACC3 V3.

~~16.~~10. Use of erdafitinib ~~an FGFR inhibitor~~ according to any one of the preceding claims, wherein the urothelial carcinoma is locally advanced or metastatic.

~~17.~~11. Use of erdafitinib ~~an FGFR inhibitor~~ according to claim 1 or 5, wherein the biological sample is blood, lymph fluid, bone marrow, a solid tumor sample, or any combination thereof.

~~18. Use of an FGFR inhibitor according to any one of the preceding claims wherein the FGFR inhibitor is erdafitinib.~~

~~19.~~12. Use of erdafitinib ~~an FGFR inhibitor~~ according to any one of the preceding claims~~claim 18~~, wherein erdafitinib is to be administered daily.

~~20.~~13. Use of erdafitinib ~~an FGFR inhibitor~~ according to any one of the preceding claims~~claim 18 or 19~~, wherein erdafitinib is to be administered orally.

~~21.~~14. Use of erdafitinib ~~an FGFR inhibitor~~ according to any one of the preceding claims ~~18 to 20~~, wherein erdafitinib is to be administered orally on a continuous daily dosing schedule.

~~22.~~15. Use of erdafitinib ~~an FGFR inhibitor~~ according to any one of the preceding claims ~~18 to 21~~, wherein erdafitinib is to be administered orally at a dose of about 8 mg once daily.

~~23.~~16. Use of erdafitinib ~~an FGFR inhibitor~~ according to any one of the preceding claims~~claim 22~~, wherein the dose of erdafitinib is to be increased from 8 mg once daily to 9 mg once daily at 14 to 21 days after initiating treatment if:

(a) the patient exhibits a serum phosphate (PO_4) level that is less than about 5.5 mg/dL or is < 7 mg/dL or ranges from and include 7 mg/dL to ≤9 mg/dL or is ≤9 mg/dL at 14-21 days after initiating treatment; and

(b) administration of erdafitinib at 8 mg once daily resulted in no ocular disorder; or

(c) administration of erdafitinib at 8 mg once daily resulted in no Grade 2 or greater adverse reaction.

17. Use of erdafitinib according to claim 16, wherein the dose of erdafitinib is to be increased from 8 mg once daily to 9 mg once daily at 14 to 21 days after initiating treatment if:

(a) the patient exhibits a serum phosphate (PO_4) level that is < 7 mg/dL or ranges from and include 7 mg/dL to ≤9 mg/dL or is ≤9 mg/dL at 14-21 days after initiating treatment; and

(b) administration of erdafitinib at 8 mg once daily resulted in no ocular disorder; or

(c) administration of erdafitinib at 8 mg once daily resulted in no Grade 2 or greater adverse reaction.

~~24.~~18. Use of erdafitinib ~~an FGFR inhibitor~~ according to any one of the preceding claims ~~18 to 23~~, wherein erdafitinib is present in a solid dosage form.

~~25.~~19. Use of erdafitinib ~~an FGFR inhibitor~~ according to claim ~~24~~18, wherein the solid dosage form is a tablet.

20. Use of erdafitinib according to claim 19, wherein the tablet comprises 3 mg, 4 mg or 5 mg of erdafitinib.