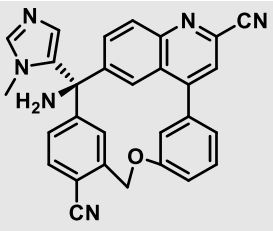
WHAT IS CLAIMED IS:

1. Use of Compound (I):



Compound (I)

or a pharmaceutically acceptable form thereof, in the manufacture of a medicament for treating squamous cell carcinoma (SCC) in a subject in combination with a PI3K inhibitor, or a pharmaceutically acceptable form thereof.

2. The use of claim 1, wherein the medicament mitigates PI3K inhibitor resistance.

3. The use of claim 2, wherein the subject is PI3K inhibitor-naïve, PI3K inhibitor relapsed, or PI3K inhibitor refractory.

4. The use of claim 1, wherein the medicament mitigates resistance to an EGFR inhibitor.

5. The use of claim 4, wherein the EGFR inhibitor is to be administered to the subject, optionally wherein the subject is EGFR inhibitor-naïve, EGFR inhibitor relapsed, or EGFR inhibitor refractory.

6. The use of claim 4 or claim 5, wherein the EGFR inhibitor is cetuximab, panitumumab, or afatinib.

7. The use of any one of claims 1 to 6, wherein the SCC is a PIK3CA-dependent SCC.

8. Use of Compound (I) or a pharmaceutically acceptable form thereof, in the manufacture of a medicament for treating PI3K-dependent SCC in a subject.

9. The use of claim 7 or claim 8, wherein the PIK3CA-dependent SCC comprises a PIK3CA mutation; optionally wherein the PIK3CA mutation is or comprises a modification in a codon that encodes an amino acid substitution at a specific position selected from a group consisting of R38, E39, E78, R88, R93, E103, P104, V105, G106, R108, E109, E110, K111, G118, P124, E218, V344, N345, D350, G364, E365, P366, C378, C420, P447, P449, H450, G451, E453, P471, P539, E542, E545, Q546, D549, E579, E600, C604, S629, V638, C901, G914, D939, E970, M1004, G1007, Y1021, T1025, D1029, E1037, M1043, N1044, H1047, G1049, A1066, and N1068, and any combination thereof, in the corresponding mutant PI3K protein, optionally wherein the PIK3CA mutation is or comprises a modification in a codon that encodes an amino acid substitution at a specific position selected from a group consisting of G118, C420, E542, E545, Q546, H1047, and any combination thereof, in the corresponding mutant PI3K protein.

10. The use of claim 8 or claim 9, wherein the PI3K-dependent SCC comprises a PIK3CA gene amplification or a PIK3CA copy gain.

11. The use of any one of claims 1 to 10, wherein the SCC is an HRAS-dependent SCC.

12. The use of claim 11, wherein the SCC comprises an HRAS mutation; optionally wherein the HRAS mutation is or comprises a modification in a codon that encodes an amino acid substitution at a specific position selected from a group consisting of G12, G13, Q61, Q22, K117, A146, and any combination thereof, in the corresponding mutant HRas protein.

13. The use of claim 11 or claim 12, wherein the SCC overexpresses wild-type HRas protein.

14. The use of any one of claims 1 to 13, wherein Compound (I), or a pharmaceutically acceptable form thereof, is to be administered orally; optionally wherein Compound (I), or a pharmaceutically acceptable form thereof, is to be administered at a dose of 0.01-50 mg/kg body weight per day, or at a dose of 0.5-2400 mg per day, or at a dose selected from about 0.5 mg, about 1 mg, about 1.5 mg, about 1.6 mg, about 1.7 mg, about 1.8 mg, about 1.9 mg, about 2 mg, about 2.5 mg, about 3 mg, about 4 mg, about 5 mg, about 6 mg, about 7 mg, about 8 mg, about 9 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg about 100 mg, about 125 mg, about 150 mg, about 175 mg, about 200 mg, about 300 mg, about 350 mg, about 400 mg, about 450 mg, about 500 mg, about 550 mg, about 600 mg, about 700 mg, about 800 mg, about 900 mg, about 1000 mg, about 1100 mg, about 1200 mg, about 1300 mg, about 1400 mg, about 1500 mg, about 1600 mg, about 1700 mg, about 1800 mg, about 1900 mg, about 2000 mg, about 2100 mg, about 2200 mg, about 2300 mg, and about 2400 mg per day; optionally wherein Compound (I), or a pharmaceutically acceptable form thereof, is to be administered 1, 2, 3, or 4 times per day, or is to be administered once per day, or is to be administered twice per day.

15. The use of any one of claims 1 to 7 or 9 to 14, wherein the PI3K inhibitor, or the pharmaceutically acceptable form thereof, is to be administered orally; optionally wherein the PI3K inhibitor is to be administered to the patient at a dose of 10 to 400 mg per day, or at a dose of about 50 mg, about 100 mg, about 150 mg, about 200 mg, about 250 mg or about 300 mg per day; optionally wherein the PI3K inhibitor is to be administered once or twice per day.

16. The use of any one of claims 1 to 15, wherein Compound (I), or a pharmaceutically acceptable form thereof, is to be administered on an interval dosing schedule, optionally wherein

the interval dosing schedule is a one week on and one week off dosing schedule, and, where the PI3K inhibitor is to be administered, said PI3K inhibitor is to be administered once per day.

17. The use of any one of claims 1 to 16, wherein the medicament delays, halts, or prevents progression of SCC and/or SCC tumor growth; optionally wherein the medicament increases Time to Progression (TTP), Progression Free Survival (PFS), Event-free survival (EFS), Overall Survival (OS), overall response rate (ORR), disease control rate (DCR), or duration of response (DoR), or increases Time to Response (TTR), or any combination thereof, compared to no therapy, chemotherapy, single agent therapy, first-line therapy, second-line therapy, anti-EGFR antibody therapy, immunotherapy, or localized and loco-regional disease therapies.

18. The use of any one of claims 1 to 7 and 9 to 17, wherein the PI3K inhibitor, or the pharmaceutically acceptable form thereof, is a PI3Kα inhibitor, or a pharmaceutically acceptable form thereof, or is selected from alpelisib (PIQRAY®; BYL719), AMG319, AZD8168, AZD8835, buparlisib, B591, CH5132799, copanlisib (aliqopa), delalisib (zydelig), duvelisib (copiktra), eganelisib, GSK2636771, leniolisib, linperlisib, parsaclisib, pictilisib, pilaralisib, RIDR-PI-103, serabelisib, sonolisib, taselisib, tenalisib, TG-100-115, umbralisib, zandelisib, ZSTK474, STX-478, RLY-2608, LOXO-783, or inavolisib, or a pharmaceutically acceptable form thereof; optionally wherein the PI3K inhibitor is alpelisib.

19. The use of any one of claims 1 to 18, wherein the SCC is early stage, advanced, relapsed, refractory, or metastatic, or is recurrent and/or metastatic; optionally wherein the SCC is HNSCC, oral cavity HNSCC, pharynx HNSCC, larynx HNSCC, tonsil HNSCC, sinonasal HNSCC, nasopharyngeal HNSCC, esophageal SCC, lung SCC, thyroid SCC, cervical SCC, urothelial SCC, bladder SCC, vaginal SCC, or prostate SCC; or the SCC is cutaneous SCC.