[0032] E24: The method of any one of E5-E22, the DLL3-binding domain comprises a VH that comprises the amino acid sequence of SEQ ID NO:11, and a VL that comprises the amino acid sequence of SEQ ID NO:12, and the CD3-binding domain comprises a VH that comprises the amino acid sequence of SEQ ID NO:21, and a VL that comprises the amino acid sequence of SEQ ID NO:22.

[0033] E25: The method of any one of E5-E23, wherein the DLL3-binding domain comprises the amino acid of SEQ ID NO:9 and the CD3-binding domain comprises the amino acid of SEQ ID NO: 23.

[0034] E26: The method of any one of E5-E21 or E24, the DLL3-binding domain comprises the amino acid of SEQ ID NO:13 and the CD3-binding domain comprises the amino acid of SEQ ID NO:23.

[0034a] E26a: In one example, the present disclosure refers to the use of an anti-DLL3 agent and an anti-PD-1 antibody in the manufacture of a medicament for combination therapy for treating small cell lung cancer (SCLC), wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NOs: 13 and 23 and an anti-PD-1 antibody, wherein the anti-DLL3 agent is to be administered at a dose of from 0.3 mg to 30 mg or from 3 mg to 100 mg once every two weeks, and wherein the SCLC recurred in the subject after at least one prior platinum-based chemotherapy.

[0034b] E26b: In another example, the present disclosure refers to the use of an anti-DLL3 agent in the manufacture of a first medicament and use of an anti-PD-1 antibody in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating small cell lung cancer (SCLC), wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NOs: 13 and 23, wherein the anti-DLL3 agent is to be administered at a dose of from 0.3 mg to 30 mg or from 3 mg to 100 mg once every two weeks, and wherein the SCLC recurred in the subject after at least one prior platinum-based chemotherapy.

[0034c] E26c: In yet another example, the present disclosure refers to the use of an anti-DLL3 agent in the manufacture of a medicament for use in combinatorial therapy for treating small cell lung cancer (SCLC), wherein said medicament is to be administered in combination with an anti-PD-1 antibody, wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NOs: 13 and 23, wherein the anti-DLL3 agent is to be administered at a dose of from 0.3 mg to 30 mg or from 3 mg to 100 mg once every two weeks, and wherein the SCLC recurred in the subject after at least one prior platinum-based chemotherapy.

[0035] E27: The method of E25, wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NO:10.

[0036] E28: The method of E27, wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NO:14.

[0037] E29: The method of any one of E5-E28, wherein the anti-DLL3 agent further comprises a third domain that extends or enhance the serum half-life of the anti-DLL3 agent.

[0038] E30: The method of E29, wherein the third domain comprises the amino acid sequence selected from any one of SEQ ID NOs:51-58.

[0039] E31: The method of any one of E5-E22, E24, E26, E28-E30, wherein the anti-DLL3 agent comprises the amino acid of SEQ ID NO:27 or 59.

[0040] E32: The method of any one of E5-E31, wherein the anti-PD-1 antibody comprises (a) a VH that comprises: (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 32, (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 33, (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 34; and (b) a VL that comprises: (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 35, (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 36, (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 37.

[0041] E33: The method of any one of E5-E32, wherein the anti-PD-1 antibody comprises a VH that comprises the amino acid sequence of SEQ ID NO: 38, and a VL that comprises the amino acid sequence of SEQ ID NO: 39.

[0042] E34: The method of any one of E5-E33, wherein the anti-PD-1 antibody comprises a heavy chain (HC) that comprises the amino acid sequence of EQ ID NO:40, and a light chain (LC) that comprises the amino acid sequence of SEQ ID NO:41.

[0043] E35: The method of any one of E1or E3-E34, wherein the anti-DLL3 agent is administered once every two weeks at a dose of: from about 0.3 mg to about 30 mg, from about 1 mg to about 30 mg, from about 3 mg to about 30 mg or from about 10 mg to about 30 mg.

[0044] E36: The method of E35, wherein the anti-DLL3 agent is administered once every two weeks at a dose of about 0.3 mg, 1 mg, 3 mg, 10 mg, 25 mg or 30 mg.

In one aspect, the present disclosure refers to use of an anti-DLL3 agent and an anti-PD-1 antibody in the manufacture of a medicament for combination therapy for treating small cell lung cancer (SCLC), wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NOs: 13 and 23, wherein the anti-DLL3 agent is to be administered at a dose of from 1 mg to 30 mg once every two weeks, and wherein the SCLC recurred in the subject after at least one prior platinum-based chemotherapy.

In another aspect, the present disclosure refers to use of an anti-DLL3 agent in the manufacture of a first medicament and use of an anti-PD-1 antibody in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating small cell lung cancer (SCLC), wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NOs: 13 and 23, wherein the anti-DLL3 agent is to be administered at a dose of from 1 mg to 30 mg once every two weeks, and wherein the SCLC recurred in the subject after at least one prior platinum-based chemotherapy.

In another aspect, the present disclosure refers to use of an anti-DLL3 agent in the manufacture of a medicament for use in combinatorial therapy for treating small cell lung cancer (SCLC), wherein said medicament is to be administered in combination with an anti-PD-1 antibody, wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NOs: 13 and 23, wherein the anti-DLL3 agent is to be administered at a dose of from 1 mg to 30 mg once every two weeks, and wherein the SCLC recurred in the subject after at least one prior platinum-based chemotherapy.

CLAIMS

What is claimed:

1. Use of an anti-DLL3 agent and an anti-PD-1 antibody in the manufacture of a medicament for combination therapy for treating small cell lung cancer (SCLC), wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NOs: 13 and 23, wherein the anti-DLL3 agent is to be administered at a dose of from 1 mg to 30 mg once every two weeks, and wherein the SCLC recurred in the subject after at least one prior platinum-based chemotherapy.

2. Use of an anti-DLL3 agent in the manufacture of a first medicament and use of an anti-PD-1 antibody in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy for treating small cell lung cancer (SCLC), wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NOs: 13 and 23, wherein the anti-DLL3 agent is to be administered at a dose of from 1 mg to 30 mg once every two weeks, and wherein the SCLC recurred in the subject after at least one prior platinum-based chemotherapy.

3. Use of an anti-DLL3 agent in the manufacture of a medicament for use in combinatorial therapy for treating small cell lung cancer (SCLC), wherein said medicament is to be administered in combination with an anti-PD-1 antibody, wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NOs: 13 and 23, wherein the anti-DLL3 agent is to be administered at a dose of from 1 mg to 30 mg once every two weeks, and wherein the SCLC recurred in the subject after at least one prior platinum-based chemotherapy.

4. The use of any one of claims 1 to 3, wherein the anti-DLL3 agent is to be administered at a dose of 3 mg, 10 mg, 25 mg or 30 mg once every two weeks.

5. The use of any one of claims 1 to 4, wherein the anti-DLL3 agent is to be administered on day 1 and day 15 of a 28-day cycle.

6. The use of claim 5, wherein the anti-PD-1 antibody is nivolumab, pembrolizumab, cemiplimab, tislelizumab, sintilimab, or zeluvalimab.

7. The use of claim 6, wherein the anti-PD-1 antibody is pembrolizumab and wherein the pembrolizumab is to be administered at a dose of 200 mg once every three weeks.

8. The use of claim 6, wherein the anti-PD-1 antibody is nivolumab and wherein the nivolumab is to be administered at a dose of 240 mg once every two weeks.

9. The use of claim 6, wherein the anti-PD-1 antibody is zeluvalimab and wherein the zeluvalimab is to be administered at a dose of 480 mg once every three weeks.

10. The use of claim 7, wherein pembrolizumab is to be administered before the anti-DLL3 agent if both are to be administered on the same day.

11. The use of any one of claims 1 to 10, the method further comprises one or more additional therapeutic agent to be administered to the subject.

12. The use of claim 11, wherein the one or more additional therapeutic agent is a corticosteroid, saline, or tocilizumab.

13. The use of claim 12, wherein the corticosteroid is dexamethasone.

14. The use of any one of claims 11 to 13, wherein the anti-DLL3 agent is to be administered in at least one cycle comprising a first cycle, and wherein the one or more additional therapeutic agent is to be administered in the first cycle wherein the anti-DLL3 agent is to be administered.

15. The use of any one of claims 1 to 14, wherein the platinum-based chemotherapy is platinum-etoposide therapy.

16. The use of any one of claims 1 to 15, wherein the anti-DLL3 agent is to be administered by IV infusion.

17. The use of any one of claims 1 to 16, wherein the subject is a human.

18. The use of any one of claims 1 to 17, wherein the anti-DLL3 agent comprises the amino acid sequence of SEQ ID NO: 27 or 59.