CLAIMS

What is claimed is:

1. A bispecific binding molecule comprising:

(a) a target protein binding domain that specifically binds to a target protein, wherein the target protein is a non-Receptor Tyrosine Kinase (non-RTK) protein; and

(b) a neuropilin-1 (NRP1) binding domain that binds to NRP1 comprising an antibody or NRP-1-binding fragment thereof,

wherein binding of the bispecific binding molecule to the target protein and to NRP1 results in lysosomal degradation of the target protein in a target cell.

2. The bispecific binding molecule of claim 1, wherein the non-RTK protein is selected from integrins, G-protein coupled receptors (GPCRs), immune checkpoint receptors, and ion channel receptors.

3. The bispecific binding molecule of claim 1, wherein the non-RTK protein is an integrin.

4. The bispecific binding molecule of claim 3, wherein the non-RTK protein is integrin αVβ.

5. The bispecific binding molecule of claim 3, wherein the non-RTK protein is integrin αVβ3.

6. The bispecific binding molecule of claim 1, wherein the non-RTK protein is a GPCR.

7. The bispecific binding molecule of claim 1, wherein the non-RTK protein is an immune checkpoint receptor.

8. The bispecific binding molecule of claim 7, wherein the immune checkpoint receptor is PD-L1.

9. The bispecific binding molecule of claim 1, wherein the non-RTK protein is an ion channel receptor.

10. The bispecific binding molecule of any one of claims 1-9, wherein the target cell is a cancer cell.

11. The bispecific binding molecule of claim 10, wherein the cancer cell is selected from the group consisting of lung cancer, breast cancer, colon and rectum cancer, head and neck cancer, esophagogastric cancer, liver cancer, glioblastoma, prostate cancer, cervical cancer, ovarian cancer, bladder cancer, kidney cancer, and pancreatic cancer.

12. The bispecific binding molecule of claim 10, wherein the cancer cell is a non-small cell lung cancer (NSCLC) cell.

13. The bispecific binding molecule of any one of claims 1-9, wherein the target protein binding domain and the NRP1 binding domain are each independently selected from the group consisting of IgG, half antibodies, single-domain antibodies, nanobodies, Fabs, monospecific Fab2, Fc, scFv, minibodies, IgNAR, V-NAR, hcIgG, VHH domain, camelid antibodies, and peptibodies.

14. The bispecific binding molecule of claim 1, wherein the NRP1 binding domain comprises:

(i) an antibody heavy chain variable (VH) domain comprising CDR1, CDR2 and CDR3 regions (HCDR1, HCDR2 and HCDR3, respectively), wherein HCDR1 consists of the sequence shown in SEQ ID NO: 79, HCDR2 consists of the sequence shown in SEQ ID NO: 80, and HCDR3 consists of the sequence shown in any one of SEQ ID NOs: 81-84; and

(ii) an antibody light chain variable (VL) domain comprising CDR1, CDR2 and CDR3 regions (LCDR1, LCDR2 and LCDR3, respectively), wherein LCDR1 consists of the sequence shown in any one of SEQ ID NOs: 85-87, LCDR2 consists of the sequence shown in SEQ ID NO: 88, and LCDR3 consists of the sequence shown in SEQ ID NO: 89.

15. The bispecific binding molecule of claim 14, wherein:

(i) HCDR1 consists of the sequence shown in SEQ ID NO: 79, HCDR2 consists of the sequence shown in SEQ ID NO: 80, and HCDR3 consists of the sequence shown in any one of SEQ ID NO: 84; and

(ii) LCDR1 consists of the sequence shown in SEQ ID NO: 85, LCDR2 consists of the sequence shown in SEQ ID NO: 88, and LCDR3 consists of the sequence shown in SEQ ID NO: 89.

16. The bispecific binding molecule of any one of claims 1-15, which is part of an antibody-drug conjugate (ADC).

17. A nucleic acid encoding the bispecific binding molecule of any one of claims 1-15.

18. An expression vector comprising the nucleic acid of claim 17.

19. A cell capable of protein expression comprising the expression vector of claim 18.

20. A use of the bispecific binding molecule of any one of claims 1-15 in the manufacture of a medicament for treating cancer in a subject.

21. Use of the bispecific binding molecule of any one of claims 1-15 in the manufacture of a medicament for inducing lysosomal degradation of a target protein in a cell, wherein the bispecific binding molecule is to be contacted with the cell such that lysosomal degradation of the target protein is to be induced in the cell.

22. The use of claim 21, wherein the cell comprises one or more mutations in the target protein and/or overexpresses the target protein.

23. The use of claim 21, wherein the target protein is an integrin.

24. The use of claim 21, wherein the target protein is a GPCR.

25. The use of claim 21, wherein the target protein is an immune checkpoint receptor.

26. The use of claim 21, wherein the target protein is an ion channel receptor.

27. The use of claim 21, wherein the cell is resistant or refractory to responsiveness to an inhibitor of the target protein.

28. Use of the bispecific binding molecule of any one of claims 1-15 in the manufacture of a medicament for inhibiting tumor growth in a subject having a tumor, wherein the bispecific binding molecule is to be administered to the subject such that growth of the tumor in the subject is to be inhibited.

29. The use of claim 28, wherein the tumor comprises one or more mutations in the target protein and/or overexpresses the target protein.

30. The use of claim 28, wherein the target protein is an integrin.

31. The use of claim 28, wherein the target protein is a GPCR.

32. The use of claim 28, wherein the target protein is an immune checkpoint receptor.

33. The use of claim 28, wherein the target protein is an ion channel receptor.

34. The use of claim 28, wherein the tumor is resistant or refractory to responsiveness to an inhibitor of the target protein.

35. The use of claim 28, wherein the bispecific binding molecule is to be administered intravenously, intraperitoneally, intrathecally, intraventricularly, or intraparenchymally.

36. The bispecific binding molecule of any one of claims 1-15 for use in therapy.