CLAIMS

WHAT IS CLAIMED IS:

1. Use of a chemical inducer of proximity (CIP) which couples B-cell lymphoma 6 (BCL-6) and either (a) a bromodomain and extra-terminal domain (BET) family protein or (b) a cyclin-dependent kinase (CDK), for the manufacture of a medicament for modulating a target gene in a cell.

2. The use of claim 1, wherein the use comprises:

(a) contacting the cell with the CIP which couples BCL-6 and the BET family protein,

wherein upon contacting the cell, BCL-6 and the BET family protein are spatially complexed to each other via the CIP to yield a gain-of-function in the cell,

wherein the gain-of-function is characterized by modulating expression of the target gene in a manner dependent on presence of the BET family protein bound to the CIP; or

(b) contacting the cell with the CIP which couples BCL-6 and CDK,

wherein upon contacting the cell, BCL-6 and CDK are spatially complexed to each other via the CIP to yield a gain-of-function in the cell,

wherein the gain-of-function is characterized by modulating expression of the target gene in a manner dependent on presence of CDK bound to the CIP,

thereby modulating the target gene.

3. The use of claim 1 or 2, wherein the CIP is a compound comprising the structure of:

A-B (Formula I); or

A-linker-B (Formula II).

4. The use of claim 3, wherein A comprises a first moiety exhibiting selective binding to BCL-6; and B comprises a second moiety exhibiting selective binding to either (a) the BET family protein or (b) the CDK.

5. The use of any one of claims 1-4, wherein the target gene is a proapoptotic gene.

6. The use of claim 5, wherein the proapoptotic gene is selected from the group consisting of: *TP53*, *PUMA* (*BBC3*), *BIM* (*BCL2L11*), *BID*, *BAX*, *BAK*, *BOK*, *BAD*, *HRK*, *BIK*, *BMF*, *NOXA*, *CASP8*, and *CASP10*.

7. The use of claim 5 or 6, wherein the modulating expression of the target gene comprises increasing expression of the proapoptotic gene in the cell.

8. The use of any one of claims 1-7, wherein the use results in apoptosis of the cell.

9. The use of any one of claims 1-8, wherein both BCL-6 and the BET family protein, or both BCL-6 and the CDK, are endogenously expressed in the cell.

10. The use of any one of claims 1-9, wherein the cell is a diseased cell.

11. The use of claim 10, wherein the diseased cell overexpresses both BCL-6 and the BET family protein, or both BCL-6 and the CDK, relative to a non-diseased cell.

12. The use of claim 10 or 11, wherein the diseased cell is a cancer cell.

13. The use of any one of claims 1-12, wherein the contacting comprises administering the CIP to a subject comprising the cell.

14. The use of claim 13, wherein the subject has a disease, a disorder, or a condition.

15. The use of claim 14, wherein the administering the CIP results in treatment of the disease, disorder, or condition, or a symptom associated therewith.

16. The use of claim 14 or 15, wherein the disease, disorder, or condition is a malignancy.

17. The use of claim 16, wherein the malignancy is small cell lung cancer (SCLC), diffuse large B-cell lymphoma (DLBCL), breast cancer, or a malignancy with high-level expression of BCL-6 protein.

18. The use of claim 17, wherein the DLBCL is refractory DLBCL.

19. The use of claim 18, wherein the refractory DLBCL is CHOP-resistant DLBCL.

20. The use of claim 16, wherein the malignancy has a mutation in TP53.

21. The use of any one of claims 13-20, wherein the subject is a human.

22. The use of any one of claims 1-21, wherein the CDK is selected from the group consisting of: CDK9, CDK8, and CDK7.

23. The use of any one of claims 1-22, wherein the BET family protein is selected from the group consisting of: BRD2, BRD3, BRD4, BRD5, BRD7, BRD9, and BRDT.

24. A chemical inducer of proximity (CIP) having the structure of:

A-B (Formula I); or

A-linker-B (Formula II),

wherein A comprises a first moiety exhibiting selective binding to B-cell lymphoma 6 (BCL-6), and

wherein B comprises a second moiety exhibiting selective binding to either:

(a) a bromodomain and extra-terminal domain (BET) family protein; or

(b) a cyclin-dependent kinase (CDK).

25. The CIP of claim 24, wherein the CDK is selected from the group consisting of: CDK9, CDK8, and CDK7.

26. The CIP of claim 24 or 25, wherein the BET family protein is selected from the group consisting of: BRD2, BRD3, BRD4, BRD5, BRD7, BRD9, and BRDT.

27. A chemical inducer of proximity (CIP) which couples B-cell lymphoma 6 (BCL-6) and either (a) a bromodomain and extra-terminal domain (BET) family protein or (b) a cyclin-dependent kinase (CDK), for use as a medicament.

28. The CIP of claim 27, wherein the CDK is selected from the group consisting of: CDK9, CDK8, and CDK7.

29. The CIP of claim 27 or 28, wherein the BET family protein is selected from the group consisting of: BRD2, BRD3, BRD4, BRD5, BRD7, BRD9, and BRDT.