LIBC No.	Domain	Sequence	SEQ ID
consensus	V_H	QVQLVESGGGVVQPGRSLRLSCAASGFTFSX$_{31}$YX$_{33}$MX$_{35}$WVRQAPGKGLEWVAX$_{50}$IX$_{52}$YDX$_{55}$X$_{56}$X$_{57}$X$_{58}$YX$_{60}$X$_{61}$DSVKGRFTISRDNSKNTLSLQMNSLRAEDTAVYYCARX$_{99}$RX$_{101}$X$_{102}$X$_{103}$X$_{104}$X$_{105}$X$_{106}$X$_{107}$YYGX$_{111}$X$_{112}$VWGQGTTVTVSS	119
	V_L	SYELTQPPSVSVSPRQTARITCSGDX$_{26}$LPX$_{29}$X$_{30}$YX$_{32}$YWYQQKPGQAPVLVIYKDNERPSGIPERFSGSSSGTTVTLTISGVQAEDEADYYCQSX$_{90}$DX$_{92}$SX$_{94}$X$_{95}$YX$_{97}$X$_{98}$FGGGTKLTVLG	120
219081 19325	V_H	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVIWYDGSNQYYADSVKGRFIISRDNSKNTLYLQMNSLRAEDTAVYYCARDRVAAHPAYYYGLDVWGQGTTVTVSS	121
	V_L	SYELTQPPSVSLSPGQTARITCSGDALPNHYAYWYQQKPGQAPVLVIFKDNERPSGIPERFSGSSSGTTVTLTISGVQAEDEADYYCQSADSSGSYVIFGGGTKLTVLG	122
218979 19319	V_H	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVIWYDGSNKYYADSVKGRFTISRDNSKNTLSLQMNSLRAEDTAVYYCARERIAAAPYYYYGMDVWGQGTTVTVSS	123
	V_L	SYELTQPPSVSVSPRQTARITCSGDALPKHYAYWYQQKPGQAPVLVIYKDNERPSGIPERFSGSSSGTTVTLTISGVQAEDEADYYCQSADNTGSYMVFGGGTKLTVLG	124
1308929	V_H	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLDWVGVIWYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDRVAARPHYYYGLDVWGQGTTVTVSS	125
	V_L	SYELTQPPSVSVSPGQTARITCSGDALPNHYAYWYQQKPGQAPVLVIYKDNERPSGIPERFSGSSSGTTVTLTISGVQAEDEADYYCQSADSSGSYVVFGGGTKLTVLG	126
1318341	V_H	LVQLVESGGGVVQPGRSLRLSCAASGFTFRSYAMHWVRQAPGKGLEWVAVIWYDGTNKYYADSVKGRFTISRDNSKNTLYLQMNTLRADDTAVYFCAKDRVAARPDYYYGMDVWGQGTTVTVSS	127
	V_L	SYELTQPPSVSVSPGQTARIACSGDALPDHYTYWYQQKPGQAPVLVIYKDNERPSGIPERFSGSSSGTTVTLTISGVQAEDEADYYCQSADSSGAYVIFGGGTKLTVLG	128
1318409	V_H	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVIWYDGSNKYYADSVKGRFTISRDNSKDTLHLQMNSLRAEDMAVYFCAKDRVVARPDYYYGMDVWGQGTTVTVSS	129
	V_L	SYELTQPPSVSVSPGQTARITCSGDALPQHYTYWYQQKPGQAPVLVIYKDNERPSGIPERFSGSSSGTTVTLTIRGVQAEDEADYYCQSADGSGTYVVFGGGTKLTVLG	130
1318412	V_H	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYAMHWVRQAPGKGLEWVAVIWYDGRKRYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDRIAARPNYYYGLDVWGQGTTVTVSS	131
	V_L	SYELIQPPSVSVSPGQTARITCSGDTLPEHYTYWYQQRPGQAPILVIYKDNERPSGIPERFSGSSSGTTVTLTIRGVQAEDEADYYCQSADSSGAYVVFGGGTKLTVLG	132
1318738	V_H	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYDMHWVRQAPGKGLEWVAVIRYDGSNKYYEDSVKGRFTISRDNSKNTLYLQMNSLRVEDTAVYYCARERGPYGGNTYYGMDVWGQGTTVTVSS	133
	V_L	SYELTQPPSVSVSPGQTARITCSGDALPKHYAYWYQQKPGQAPVMVIYKDNERPSGIPERFSGSSSGTTVTLTISGVQAEDEADYYCQSTDSSATYVVFGGGTKLTVLR	134
1319003	V_H	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVIWYDGRKRYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDRIAARPNYYYGLDVWGQGTTVTVSS	135

N, or S; the LCDR2 amino acid sequence of EVX_3X_4RPS (SEQ ID NO: 279), where X_3 is T or S and X_4 is K or V; and the LCDR3 amino acid sequence of $CSYX_4X_5SX_7TX_9V$ (SEQ ID NO: 280), where X_4 is A or V; X_5 is D or E; X_7 is S or K; X_9 is L or W. Light chain CDR sequences of exemplary agonist LTβR binding proteins that bind to human LTβR CRD4, do not block LIGHT binding to LTβR, do not block LTα1β2 binding to LTβR, and comprise a LCDR1 of SEQ ID NO: 278, a LCDR2 of SEQ ID NO: 279, and a LCDR3 of SEQ ID NO: 280 are provided in Table 7 below.

[0140] In one embodiment, the agonist LTβR binding proteins of the present disclosure comprising the HCDRs 1–3 of SEQ ID NOs. 159-161, respectively, further comprise a shared VL CDR structure defined by the LCDR1 amino acid sequence of $SGDX_4LPX_7X_8YX_{10}Y$ (SEQ ID NO: 308), where X_4 is A or T; X_7 is Q, E, N, R, or K; X_8 is H or Q; X_{10} is V, T, or A; the LCDR2 amino acid sequence of KDX_3X_4RPS (SEQ ID NO: 309) where X_3 is N or S; X_4 is D or E; and the LCDR3 amino acid sequence of $QSADX_5SGX_8X_9VV$ (SEQ ID NO: 310), where X_5 is I, N, or S; X_8 is S, A, I, or T; and X_9 is F or Y. Light chain CDR sequences of exemplary agonist LTβR binding proteins that bind to human LTβR CRD4, do not block LIGHT binding to LTβR, do not block LTα1β2 binding to LTβR, and comprise a LCDR1 of SEQ ID NO: 308, a LCDR2 of SEQ ID NO: 309, and a LCDR3 of SEQ ID NO: 310 are provided in Table 7 below.

TABLE 6. Heavy Chain CDR Sequences of agonist LTβR binding proteins that bind human LTβR CRD4 and do not block LIGHT or LTα1β2 binding to LTβR

LIBC No.	HCDR1		HCDR2		HCDR3	
	SEQ	ID	SEQ	ID	SEQ	ID
Consensus VH Clade 1	GX_2YMH X_2 is Y or F	159	$WINPNX_6GGTNYAQKFQG$ X_6 is S, N, or R	160	$X_1X_2X_3X_4GX_6X_7X_8YYGMDV$ X_1 is D, A X_2 is R, D X_3 is N, S, A X_4 is G, S X_6 is V, W X_7 is Y, ABSENT X_8 is Y, ABSENT	161
1303255	GYYMH	162	WINPNNGGTNYAQKFQG	163	ADNSGWYYYYGMDV	164
1303574	GYYMH	165	WINPNNGGTNYAQKFQG	166	ADNSGWYYYYGMDV	167
1303613	GYYMH	168	WINPNNGGTNYAQKFQG	169	ADNSGWYYYYGMDV	170
1303507	GYYMH	171	WINPNNGGTNYAQKFQG	172	ADNSGWYYYYGMDV	173
1303716	GYYMH	174	WINPNNGGTNYAQKFQG	175	ADNSGWYYYYGMDV	176
1308640	GYYMH	177	WINPNNGGTNYAQKFQG	178	ADSSGWYYYYGMDV	179
1308591	GFYMH	180	WINPNNGGTNYAQKFQG	181	ADSSGWYYYYGMDV	182
1303446	GYYMH	183	WINPNNGGTNYAQKFQG	184	ADNSGWYYYYGMDV	185
1306164	GYYMH	186	WINPNSGGTNYAQKFQG	187	DRAGGVYYGMDV	188
1306253	GYYMH	189	WINPNRGGTNYAQKFQG	190	DRAGGVYYGMDV	191
1306424	GYYMH	192	WINPNRGGTNYAQKFQG	193	DRAGGVYYGMDV	194
Consensus VH Clade 4	X_1YGMH X_1 is A or S	195	$X_1IWYDGNNKYYX_{12}DSVKG$ X_1 is L or V X_{12} is E or A	196	$DRITX_5VRGVTNYGMDV$ X_5 is M, R	197
1306053	AYGMH	200	LIWYDGNNKYYADSVKG	198	DRITRVRGVTNYGMDV	199
1306153	AYGMH	200	LIWYDGNNKYYADSVKG	201	DRITRVRGVTNYGMDV	202
1306251	AYGMH	203	LIWYDGNNKYYADSVKG	204	DRITRVRGVTNYGMDV	205
1306674	AYGMH	206	LIWYDGNNKYYADSVKG	207	DRITRVRGVTNYGMDV	208

[0158] As described in the Examples herein, paratope mapping studies of several LTβR antibodies disclosed herein showed that, in some cases, binding of a particular LTβR antibody to LTβR did not involve or require all three heavy chain CDR regions of the antibody and/or did not involve all residues of one or more heavy chain CDRs. Heavy chain CDRs shown not to be involved in the LTβR antibody binding interaction are indicated with an asterisk in Table 10 below. Residues of heavy chain CDR regions shown not to be involved in or required for the LTβR antibody binding interaction as identified by paratope mapping or mutational analysis are identified as variable residue (X). The identity of X residues within the sequences of Table 10 is provided in Tables 18-25 herein.

Table 10. Heavy Chain CDR Sequences of LTβR Binding Proteins

LIBC No.	Well ID	HCDR1		HCDR2		HCDR3	
		SEQ	ID	SEQ	ID	SEQ	ID
218990 (19320)	30H1	GDYMY*	475	WINPX$_5$SGGTNX$_{11}$–X$_{17}$	499	EGSSGWSAEYX$_{11}$X$_{12}$X$_{13}$	529
				WINPX$_5$SGGTNX$_{11}$–X$_{17}$	500	EGSSGWSAEYX$_{11}$X$_{12}$X$_{13}$	530
				WINPNSGGTNYAKKFQG	501	EGSSGWSAEYFQH	531
218994 (19321)	31A3	SYX$_3$X$_4$ X$_5$	476	IIWYX$_5$X$_6$SDX$_9$–X$_{17}$	502	GDSEDFYYYDX$_{11}$X$_{12}$X$_{13}$	532
		SYX$_3$X$_4$ X$_5$	477	IIWYX$_5$X$_6$SDX$_9$–X$_{17}$	503	GDSEDFYYYDX$_{11}$X$_{12}$X$_{13}$	533
		SYGMH	478	IIWYDGSDEYYADSVKG	504	GDSEDFYYYDFDV	534
219058 (19324)	36G2	TSGMN	479	SVSSSGSYX$_9$–X$_{17}$	505	AX$_2$YNWHFDASX$_{11}$X$_{12}$	535
				SVSSSGSYX$_9$–X$_{17}$	506	AX$_2$YNWHFDASX$_{11}$X$_{12}$	536
				SVSSSGSYIYYADSVKG	507	ARYNWHFDASDI	537
219037 (19322)	34D1	SGGYFWS	480	YSHYSGTTYYNPSLKS	508	VPDGEDYFDY	538
219098 (19327)	44B1	SYAMS	481	TISGSGGSTYYADSVKG	509	VRDNWNYX$_8$X$_9$MDV	539
						VRDNWNYX$_8$X$_9$MDV	540
						VRDNWNYDGMDV	541
219098.001		SYAMS	482	TISGSGGSTYYADSVKG	510	VRDNWNYDGMDV	542
219097 (19326)	43D9	DAWX$_9$X$_{10}$	740	RIKTKTDGGTTDYAAPVKG*	743	DYGDYX$_6$X$_7$	744
		DAWX$_9$X$_{10}$	741			DYGDYX$_6$X$_7$	745
		DAWMS	742			DYGDYEY	746
219051 (19323)	35F5	GYYLH	483	WINPNIGVTDX$_{11}$AQKFQD	511	RGYNDDYDFDY	543
				WINPNIGVTDX$_{11}$AQKFQD	512		
				WINPNIGVTDSAQKFQD	513		
218989-1	29G8	TSGMGVG	484	LIYWNGGKLYSPSLKN	514	SGYYDNSGYYWDGMDV	544
218967	17F5	SYFWT	485	YIYYSGSTNYNPSLKS	515	VETIMAFDAFDI	545
218981	25C9	SGGYFWS	486	YTHYIGSTYYNPSLKS	516	VDTAMVDAFDI	546
218995	31C9	SRNWWG	487	YIHYIGNTYYNPSLKS	517	ETGSDGDDTFDI	547
218996	31B10	NYDMH	488	TIWYDGSNKYYADSVKG	518	LSTVTTGDYYGMDV	548
218998	32A2	SGGYFWG	489	YIHYIGSPYYNPSLKS	519	DCSSVNCQDAFDI	549
219083	41H7	SDGYFWS	490	FIYYSGTTYYNPSLKS	520	VCGGDCYDAFDI	550
219092	43C1	NSIWWG	491	YIHYSGNTYYNPSLKS	521	NFGDVDAFDI	551
219023	33G6	SNSAAWN	492	RTYCRSKCYSDYALSVKS	522	AVADHYSYALDV	552
219023.001		SNSAAWN	493	RTYYRSKWYSDYALSVKS	523	AVADHYSYALDV	553
219095	43G5	NYAMN	494	VISDSGGSSNYADSVKG	524	DRSIAGYYGMDV	554
219102	44G11	SYYWS	495	YIYYGGSTNYNPSLKS	525	SYSSAWYGSAY	555

SYA X_4X_5 X_4 is M, H, Q, Y, F, L, I, V X_5 is H, D, E, N, M, R, Q	928	VIWYDGSNQYX$_{11}$–X$_{17}$ X_{11} is Y, H, M I, L, F, W X_{12} is A, G, S, T, V X_{13} is D, S, K, Q, H, N, E X_{14} is S, G, D, E, N, Q, A, T X_{15} is V, T, A, M, F, L, I X_{16} is K, D, E, N, Q, R X_{17} is G, A, S, N	931	DRVAAHPAYYX$_{11}$–X$_{15}$ X_{11} is Y, H, M I, L, F, W X_{12} is G, A, S, N X_{13} is L, M, V, I , Y, F X_{14} is D, S, K, Q, H, N, E X_{15} is V, T, A, M, F, L, I	934
SYAMH	8	VIWYDGSNQYYADSVKG	9	DRVAAHPAYYYGLDV	10
LCDR1	**ID**	**LCDR2**	**ID**	**LCDR3**	**ID**
X_1X_2DALPX$_7X_8$YAY X_1, X_2, X_7, X_8 are each independently any amino acid residue	932	KDNERPS	66	QSADX$_5$SGSYVI X_5 is any amino acid residue	936
X_1X_2DALPX$_7X_8$YAY X_1 is S, G, D, E, N, Q, A, T X_2 is G, A, S, N X_7 is N, G, D, T, S, R, K, H, E, Q, preferably N, E, or Q X_8 is H, D, E, N, M, R, Q, preferably H or Q X_7 and X_8 are each hotspot residues as defined in Table 17 above for this antibody (i.e., N33 and H39).	935			QSADX$_5$SGSYVI X_5 is S, G, D, E, N, Q, A, T, I, preferably S, A, or I X_5 is a hotspot residue as defined in Table 17 above for this antibody (i.e., S111).	937
SGDALPNHYAY	65			QSADSSGSYVI	67

Table 22. Summary of Key CDR Residues for LTβR Antibody LIBC219097 (19326/ 43D9)					
HCDR1	**ID**	**HCDR2**	**ID**	**HCDR3**	**ID**
DAWX$_9$X$_{10}$ X_9 and X_{10} are any amino acid residue	740	RIKTKTDGGTTDYAAPVKG ***not part of paratope***	743	DYGDYX$_6$X$_7$ X_6 and X_7 are any amino acid residue	744
DAWX$_9$X$_{10}$ X_9 is M, H, Q, Y, F, L, I, V X_{10} is S, G, D, E, N, Q, A, T	741			DYGDYX$_6$X$_7$ X_6 is E, P, D, S, R, K, Q, H, N X_7 is Y, H, M I, L, F, W	745
DAWMS	742			DYGDYEY	746
LCDR1	**ID**	**LCDR2**	**ID**	**LCDR3**	**ID**
RTSQSISRYLN	566	GASSLX$_6$X$_7$	597	HQSYSTPPT	624

CLAIMS

1. An agonist Lymphotoxin β Receptor (LTβR) binding protein, wherein said binding protein binds an epitope comprising one or more residues of human LTβR cysteine-rich domain 4 (CRD4), wherein human LTβR CRD4 comprises amino acid residues 169-211 of SEQ ID NO: 1, and wherein said binding protein (a) does not inhibit LIGHT binding to LTβR or (b) does not inhibit LTα1β2 binding to LTβR.

2. The agonist LTβR binding protein of claim 1, wherein said binding protein (a) does not inhibit LIGHT binding to LTβR and (b) does not inhibit LTα1β2 binding to LTβR.

3. The agonist LTβR binding protein of claim 1, wherein the epitope comprises one or more residues of LTβR CRD4 at positions 197-209 of SEQ ID NO: 1.

4. The agonist LTβR binding protein of any one of claims 1–3, wherein inhibition of LIGHT and/or LTα1β2 binding to LTβR in the presence of the agonist LTβR binding protein is measured in a cell-based receptor-ligand binding assay, said assay comprising the steps of:

incubating LTβR expressing cells with media containing the agonist LTβR binding protein for 1 hour;

contacting the LTβR expressing cells, after said incubating, with a detectable LIGHT ligand, a detectable LTα1β2 ligand, or a combination thereof to allow the detectable ligands to bind to LTβR;

detecting, after said contacting, the detectable LIGHT and/or LTα1β2 ligands bound to LTβR expressing cells in the presence of the LTβR binding protein; and

identifying the agonist LTβR binding protein as not inhibiting LIGHT or LTα1β2 binding to LTβR based on said detecting.

5. The agonist LTβR binding protein of any one of claims 1–3, wherein said binding protein comprises:

a heavy chain variable domain (VH) amino acid sequence having at least 90% sequence identity to SEQ ID NO: 121 or SEQ ID NO: 123 and

a light chain variable domain (VL) amino acid sequence having at least 90% sequence identity to SEQ ID NO: 122 or SEQ ID NO: 124.

6. The agonist LTβR binding protein of any one of claims 1–3, wherein said binding protein comprises:

a VH amino acid sequence having at least 90% sequence identity to SEQ ID NO: 121 and SEQ ID NO: 123, and

a VL amino acid sequence having at least 90% sequence identity to SEQ ID NO: 122 and SEQ ID NO:124.

7. The agonist LTβR binding protein of any one of claims 1–3, wherein said binding protein comprises:

a VH amino acid sequence having at least 95% sequence identity to SEQ ID NO: 121 and SEQ ID NO: 123, and

a VL amino acid sequence having at least 95% sequence identity to SEQ ID NO: 122 and SEQ ID NO:124.

8. The agonist LTβR binding protein of any one of claims 1–7, wherein said binding protein comprises:

a VH comprising the HCDR1 amino acid sequence of $X_1YX_3MX_5$ (SEQ ID NO: 5), wherein X_1 is S or N; X_3 is G, D, or A; and X_5 is H or Y; the HCDR2 amino acid sequence of $X_1IX_3YDX_6X_7X_8X_9Y$ $X_{11}X_{12}$DSVKG (SEQ ID NO: 6), wherein X_1 is A or V; X_3 is W or R; X_6 is E or G; X_7 is S, R, or T; X_8 is N or K; X_9 is K, R, or Q; X_{11} is H or Y; and X_{12} is A or E; and the HCDR3 amino acid sequence of $X_1RX_3X_4X_5X_6$ $X_7X_8X_9YYGX_{13}X_{14}V$ (SEQ ID NO: 7), wherein X_1 is D or E; X_3 is V, G, or I; X_4 is V, P, or A; X_5 is A, Y, or G; X_6 is R, A, G, or H; X_7 is P or G; X_8 is G, N, D, Y, A or H; X_9 is Y, T, or F; X_{13} is L or M; and X_{14} is D or A;

a VL comprising the LCDR1 amino acid sequence of $SGDX_4LPX_7X_8YX_{10}Y$ (SEQ ID NO: 62), wherein X_4 is A or T; X_7 is E, K, Q, D or N; X_8 is Q or H; and X_{10} is A or T; the LCDR2 amino acid sequence of KDNERPS (SEQ ID NO: 63); and the LCDR3 amino acid sequence of $QSX_3DX_5SX_7X_8YX_{10}X_{11}$ (SEQ ID NO: 64), wherein X_3 is A or T; X_5 is S, G, or N; X_7 is G or A; X_8 is T, S, or A; X_{10} is V or M; and X_{11} is I or V.

9. The agonist LTβR binding protein of any one of claims 1–8, wherein said binding protein comprises:

a VH amino acid sequence having at least 90% sequence identity to SEQ ID NO: 121 and a HCDR1 amino acid sequence of SEQ ID NO: 5, a HCDR2 amino acid sequence of SEQ ID NO: 6, and a HCDR3 amino acid sequence of SEQ ID NO: 7; and

a VL amino acid sequence having at least 90% sequence identity to SEQ ID NO: 122 and a LCDR1 amino acid sequence of SEQ ID NO: 62, a LCDR2 amino acid sequence of SEQ ID NO: 63, and a LCDR3 amino acid sequence of SEQ ID NO: 64.

10. The agonist LTβR binding protein of any one of claims 1–9, wherein said binding protein comprises:

a VH comprising the HCDR1, HCDR2, and HCDR3 of amino acid sequences of SEQ ID NO: 11-13, respectively, and a VL comprising the LCDR1, LCDR2, and LCDR3 amino acid sequences of SEQ ID NO: 68-70, respectively; or

a VH comprising the HCDR1, HCDR2, and HCDR3 of amino acid sequences of SEQ ID NO: 8-10, respectively, and a VL comprising the LCDR1, LCDR2, and LCDR3 amino acid sequences of SEQ ID NO: 65-67, respectively.

11. The agonist LTβR binding protein of any one of claims 1–10, wherein the binding protein is an antibody.

12. The agonist LTβR binding protein of any one of claims 1–10, wherein the binding protein is a bispecific binding protein.

13. A bispecific Lymphotoxin β Receptor (LTβR) binding protein, said binding protein comprising:

an LTβR binding domain, wherein the LTβR binding domain binds an epitope comprising one or more residues of human LTβR cysteine-rich domain 4 (CRD4), wherein said LTβR CRD4 comprises amino acid residues 169-211 of SEQ ID NO: 1; and

a tumor-associated antigen binding domain,

wherein the bispecific binding protein agonizes LTβR activity, and (a) does not inhibit LIGHT binding to LTβR or (b) does not inhibit LT1α2β binding to LTβR.

14. The bispecific agonist LTβR binding protein of claim 13, wherein said binding protein (a) does not inhibit LIGHT binding to LTβR and (b) does not inhibit LTα1β2 binding to LTβR.

15. The bispecific agonist LTβR binding protein of claim 13, wherein the epitope comprises one or more residues of LTβR CRD4 at positions 197-209 of SEQ ID NO: 1.

16. The bispecific agonist LTβR binding protein of any one of claims 13–15, wherein inhibition of LIGHT and/or LTα1β2 binding to LTβR in the presence of the bispecific agonist LTβR binding protein is measured in a cell-based receptor-ligand binding assay, said assay comprising the steps of:

incubating LTβR expressing cells with media containing the bispecific agonist LTβR binding protein for 1 hour;

contacting the LTβR expressing cells, after said incubating, with a detectable LIGHT ligand, a detectable LTα1β2 ligand, or a combination thereof to allow the detectable ligands to bind to LTβR;

detecting, after said contacting, the detectable LIGHT and/or LTα1β2 ligands bound to LTβR expressing cells in the presence of the bispecific agonist LTβR binding protein; and

identifying the bispecific agonist LTβR binding protein as not inhibiting LIGHT or LTα1β2 binding to LTβR based on said detecting.

17. The bispecific agonist LTβR binding protein of claim 13, wherein the LTβR binding domain comprises:

a VH amino acid sequence having at least 90% sequence identity to SEQ ID NO: 121 or SEQ ID NO: 123, and

a VL amino acid sequence having at least 90% sequence identity to SEQ ID NO: 122 or SEQ ID NO: 124.

18. The bispecific agonist LTβR binding protein of claim 13, wherein the LTβR binding domain comprises:

a VH amino acid sequence having at least 90% sequence identity to SEQ ID NO: 121 and SEQ ID NO: 123 and

a VL amino acid sequence having at least 90% sequence identity to SEQ ID NO: 122 and SEQ ID NO: 124.

19. The bispecific agonist LTβR binding protein of claim 13, wherein the LTβR binding domain comprises:

a VH amino acid sequence having at least 95% sequence identity to SEQ ID NO: 121 and SEQ ID NO: 123 and

a VL amino acid sequence having at least 95% sequence identity to SEQ ID NO: 122 and SEQ ID NO: 124

20. The bispecific agonist LTβR binding protein of any one of claims 13–19, wherein the LTβR binding domain comprises:

a VH comprising the HCDR1 amino acid sequence of $X_1YX_3MX_5$ (SEQ ID NO: 5), wherein X_1 is S or N; X_3 is G, D, or A; and X_5 is H or Y; the HCDR2 amino acid sequence of $X_1IX_3YDX_6X_7X_8X_9Y$ $X_{11}X_{12}$DSVKG (SEQ ID NO: 6), wherein X_1 is A or V; X_3 is W or R; X_6 is E or G; X_7 is S, R, or T; X_8 is N or K; X_9 is K, R, or Q; X_{11} is H or Y; and X_{12} is A or E; and the HCDR3 amino acid sequence of $X_1RX_3X_4X_5X_6$ $X_7X_8X_9YYGX_{13}X_{14}V$ (SEQ ID NO: 7), wherein X_1 is D or E; X_3 is V, G, or I; X_4 is V, P, or A; X_5 is A, Y, or G; X_6 is R, A, G, or H; X_7 is P or G; X_8 is G, N, D, Y, A or H; X_9 is Y, T, or F; X_{13} is L or M; and X_{14} is D or A;

a VL comprising the LCDR1 amino acid sequence of $SGDX_4LPX_7X_8YX_{10}Y$ (SEQ ID NO: 62), wherein X_4 is A or T; X_7 is E, K, Q, D or N; X_8 is Q or H; and X_{10} is A or T; the LCDR2 amino acid sequence of KDNERPS (SEQ ID NO: 63); and the LCDR3 amino acid sequence of $QSX_3DX_5SX_7X_8YX_{10}X_{11}$ (SEQ ID NO: 64), wherein X_3 is A or T; X_5 is S, G, or N; X_7 is G or A; X_8 is T, S, or A; X_{10} is V or M; and X_{11} is I or V.

21. The bispecific agonist LTβR binding protein of any one of claims 13–20, wherein said binding protein comprises:

a VH amino acid sequence having at least 90% sequence identity to SEQ ID NO: 121 and a HCDR1 amino acid sequence of SEQ ID NO: 5, a HCDR2 amino acid sequence of SEQ ID NO: 6, and a HCDR3 amino acid sequence of SEQ ID NO: 7; and

a VL amino acid sequence having at least 90% sequence identity to SEQ ID NO: 122 and a LCDR1 amino acid sequence of SEQ ID NO: 62, a LCDR2 amino acid sequence of SEQ ID NO: 63, and a LCDR3 amino acid sequence of SEQ ID NO: 64.

22. The bispecific agonist LTβR binding protein of claim 13, wherein

the VH comprises the HCDR1, HCDR2, and HCDR3 of amino acid sequences of SEQ ID NO: 11-13, respectively, and the VL comprises the LCDR1, LCDR2, and LCDR3 amino acid sequences of SEQ ID NO: 68-70, respectively; or

the VH comprises the HCDR1, HCDR2, and HCDR3 of amino acid sequences of SEQ ID NO: 8-10, respectively, and the VL comprises the LCDR1, LCDR2, and LCDR3 amino acid sequences of SEQ ID NO: 65-67, respectively.

23. The bispecific agonist LTβR binding protein of any one of claims 13–22, wherein the bispecific binding protein comprises only one LTβR binding domain.

24. The bispecific agonist LTβR binding protein of any one of claims 13–22, wherein the LTβR binding domain is a Fab.

25. The bispecific agonist LTβR binding protein of any one of claims 13–24, wherein binding protein comprises one tumor-associated antigen binding domain.

26. The bispecific agonist LTβR binding protein of claim 25, wherein the tumor-associated antigen binding domain is a Fab.

27. The bispecific agonist LTβR binding protein of any one of claims 13-24, wherein binding protein comprises two tumor-associated antigen binding domains.

28. The bispecific agonist LTβR binding protein of any one of claims 13–22, wherein the LTβR binding domain is a Fab and the tumor-associated antigen binding domain is a Fab.

29. The bispecific agonist LTβR binding protein of any one of claims 13–28, wherein the LTβR binding domain and the tumor-associated antigen binding domain are each coupled to an Fc portion.

30. The bispecific agonist LTβR binding protein of claim 29, wherein the Fc portion does not bind to an Fc-gamma receptor.

31. A polynucleotide encoding the agonist LTβR binding protein of any one of claims 1–12.

32. A vector comprising the polynucleotide of claim 31.

33. A host cell comprising the polynucleotide of claim 31 or the vector of claim 32.

34. One or more polynucleotides encoding the bispecific agonist LTβR binding protein of any one of claims 13–30.

35. A vector comprising the one or more polynucleotides of claim 34.

36. A host cell comprising the one or more polynucleotides of claim 34 or the vector of claim 35.

37. A pharmaceutical composition comprising:

the agonist LTβR binding protein of any one of claims 1–12, the bispecific agonist LTβR binding protein of any one of claims 13–30, the one or more polynucleotides of claims 31 or 34, or the vector of claims 32 or 35, and

a pharmaceutically acceptable carrier.

38. The agonist LTβR binding protein of any one of claims 1–12 for use as a medicament.

39. Use of the agonist LTβR binding protein of any one of claims 1–12 in the manufacture of a medicament for treating cancer.

40. The bispecific agonist LTβR binding protein of any one of claims 13–30 for use as a medicament.

41. Use of the bispecific agonist LTβR binding protein of any one of claims 13–30 in the manufacture of a medicament for treating cancer.

42. Use of an agonist Lymphotoxin β Receptor (LTβR) binding protein in the manufacture of a medicament for treating cancer, wherein said binding protein binds an epitope comprising one or more residues of human LTβR cysteine-rich domain 4 (CRD4), wherein human LTβR CRD4 comprises amino acid residues 169-211 of SEQ ID NO: 1, and wherein said binding protein (a) does not inhibit LIGHT binding to LTβR or (b) does not inhibit LTα1β2 binding to LTβR.

43. Use of a bispecific Lymphotoxin β Receptor (LTβR) binding protein in the manufacture of a medicament for treating cancer, said binding protein comprising:

an LTβR binding domain, wherein the LTβR binding domain binds an epitope comprising one or more amino acid residues of human LTβR cysteine-rich domain 4 (CRD4), wherein human LTβR CRD4 comprises amino acid residues 169-211 of SEQ ID NO: 1; and

a tumor-associated antigen binding domain,

wherein the bispecific binding protein agonizes LTβR activity, and (a) does not inhibit LIGHT binding to LTβR or (b) does not inhibit LT1α2β binding to LTβR.

44. The use of claim 42 or claim 43 further comprising:

administering an immunomodulatory therapeutic in conjunction with said agonist LTβR binding protein or bispecific LTβR binding protein.

45. The use of claim 40, wherein the subject has a solid tumor selected from the group consisting of mesothelioma, a pancreatic tumor, an ovarian tumor, a lung tumor, an esophageal tumor, a gastric tumor, a hepatic tumor, a colorectal tumor, a cervical tumor, an endometrial tumor, a breast tumor, a renal tumor, a bladder tumor, a testicular tumor, a prostate tumor, a brain tumor, a bone tumor, and a head and neck tumor.