

The present disclosure also provides LAG3 binders that bind to LAG3 comprising CDR1 comprising the amino acid sequence GRTFSDYVMG (SEQ ID NO: 65); CDR2 comprising the amino acid sequence AISESGGRTH (SEQ ID NO: 66); and CDR3 comprising the amino acid sequence TLLWWTSEYAPIKANDYDY (SEQ ID NO: 67), *e.g.*, comprising the amino acid sequence: EVQLVE SGGGVVQPGG SLRLSCAASG RTFSDYVMGW FRQAPGKERE FVA AISESGG RTHYADSVKG RFTISRDN SK NTLYLQMN SL RPEDTALYYC ATLLWWTSE YAPIKANDYD YWGQGLTVTV SS (SEQ ID NO: 64).

~~In one aspect, there is provided a multispecific binder comprising:~~

~~(a) an immunoglobulin single variable domain (ISVD) that binds to programmed cell death protein 1 (PD1) comprising~~

~~a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 3 or SEQ ID NO: 6; a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 4 wherein X is W or V or SEQ ID NO: 7 wherein X is W or V; and~~

~~a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 5 wherein X is W or F;~~

~~and~~

~~(b) an ISVD that binds to lymphocyte activation gene 3 (LAG3) comprising: a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 65 or amino acids 6-10 of SEQ ID NO: 65; a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 66 or amino acids 1-10 of SEQ ID NO: 66; and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 67~~

In one aspect, there is provided a multispecific binder comprising an immunoglobulin single variable domain (ISVD) that binds PD1 and an ISVD that binds LAG3, wherein the ISVD that binds to PD1 comprises the amino acid sequence:

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYY

ADSVKGRFTISRDN SKNTVYLQMN SLRPEDTALYYCAGDKHQSSWYDYWGQGLTVTVSS (SEQ ID NO: 57) or said sequence optionally comprising a D1E mutation;

EVQLVESGGGLVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDN SKNT VYLQMN SLRPEDTAIYYCAGDKHQSSWYDYWGQGLTVTVSS (SEQ ID NO: 98) or said sequence optionally comprising a E1D mutation;

EVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDN SKNT VYLQMN SLRPEDTALYYCAGDKHQSSWYDYWGQGLTVTVSS (SEQ ID NO: 99) or said sequence optionally comprising a E1D mutation;

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDN SKNT

VYLQMNSLRPEDTALYYCAGDKHQSSWYDYGQGT LVTVSS (SEQ ID NO: 103) or said sequence

optionally comprising a D1E and/or N73S mutation;

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DQSKNT

5 VYLQMNSLRPEDTALYYCAGDKHQSSFYDYGQGT LVTVSS(SEQ ID NO: 104) or said sequence

optionally comprising a D1E mutation;

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DPSKNT

VYLQMNSLRPEDTALYYCAGDKHQSSFYDYGQGT LVTVSS(SEQ ID NO: 105) or said sequence

optionally comprising a D1E mutation;

10 DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DPSKNT

VYLQMNSLRPEDTALYYCAGDKHQSSFYDYGQGT LVTVSS (amino acids 1-119 of SEQ ID NO: 113) or

said sequence optionally comprising a D1E mutation;

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DQSKNT

VYLQMNSLRPEDTALYYCAGDKHQSSFYDYGQGT LVTVSS (amino acids 1-119 of SEQ ID NO: 117) or

15 said sequence optionally comprising a D1E mutation; or

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR

DSSKNTVYLQMNSLRPEDTALYYCAGDKHQSSFYDYGQGT LVTVSS (amino acids 1-119 of SEQ ID NO:

121) or said sequence optionally comprising a D1E mutation.

In another aspect, there is provided a multispecific binder comprising an ISVD that binds

20 PD1 and an ISVD that binds LAG3 wherein

(a) the ISVD that binds to PD1 comprises the amino acid sequence

DVQLVESGGG VVQPGGSLRL SCAASGSIAS IHAMGWFRQA PGKEREFVAV ITWSGGITYY

ADSVKGRFTI SRDN SKNTVY LQMNSLRPED TALYYCAGDK HQSSWYDYG QGT LVTVSS

(SEQ ID NO: 57);

25 EVQLVESGGGLVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDN SKNT

VYLQMNSLRPEDTAIYYCAGDKHQSSWYDYGQGT LVTVSS

(SEQ ID NO: 98);

EVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDN SKNT

VYLQMNSLRPEDTALYYCAGDKHQSSWYDYGQGT LVTVSS

30 (SEQ ID NO: 99);

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDN SKNT

VYLQMNSLRPEDTALYYCAGDKHQSSWYDYGQGT LVTVSS

(amino acids 1-119 of SEQ ID NO: 101);

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISRDN SKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS

(SEQ ID NO: 103);

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DQSKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS

(SEQ ID NO: 104); or

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DPSKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS

(SEQ ID NO: 105); and,

(b) the ISVD that binds to LAG3 comprises the amino acid sequence
EVQLVE SGGGVVQPGG SLRLSCAASG RTFSDYVMGW FRQAPGKERE FVAAISESGG RTHYADSVKG
RFTISRDN SK NTLYLQMNSL RPEDTALYYC ATTLLWWTSE YAPIKANDYD YWGQGT LVTV SS

(SEQ ID NO: 64); or

DVQLVESGGGVVQPGGSLRLSCAASGR TFS DYVMGWFRQAPGKEREFVAAISESGGRTHYADSVKGRFTISR DN SKNT
LYLQMNSLRPEDTALYYCATTLLWWTSEYAPIKANDYDYWGQGT LVTVSS

(amino acids 1-128 of SEQ ID NO: 96).

In another aspect, there is provided a multispecific binder that binds PD1 and LAG3 comprising:

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 98;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 98;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 63;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 63;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a human serum albumin (HSA) ISVD comprising the amino acid sequence set forth in
SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 99;

- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 20 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 99;
- a 20 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 20 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 20 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 9 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 99;
- a 9 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 20GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 20GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105 (wherein the Asp at position 1 is replaced with a Glu);
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105 (wherein the Asp at position 1 is substituted with a Glu);
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104 (wherein the Asp at position 1 is replaced with a Glu);
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;

- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

5 or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104 (wherein the Asp at position 1 is replaced with a Glu);

10

- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

15 or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;

20

- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;

25

- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine

or

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asn at position 73 is replaced with Ser);
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO:103 (wherein the Asp at position 1 is replaced with Glu and the Asn at position 73 is replaced with Ser);
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asn at position 73 is replaced with Ser);
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO:103 (wherein the Asp at position 1 is replaced with Glu and the Asn at position 73 is replaced with Ser);
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asn at position 73 is replaced with Ser);
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asn at position 73 is replaced with Ser);
 - a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
 - a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
 - a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
 - a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
 - a C-terminal Alanine
- wherein said residue numbers are Kabat residue numbers.

The PD1 and LAG3 binders may be in a single molecule such as a PD1/LAG3 binder, which is part of the present disclosure, that binds to PD1 and LAG3 that comprises: a PD1 binder comprising: CDR1 comprising the amino acid sequence `IHAMG` (SEQ ID NO: 3) or `GSIASIHAMG` (SEQ ID NO: 6); CDR2 comprising the amino acid sequence `VITXSGGITYYADSVKG` (SEQ ID NO: 4; wherein X is W or V) or `VITXSGGITY` (SEQ ID NO: 7; wherein X is W or V); and CDR3 comprising the amino acid sequence `DKHQSSXYDY` (SEQ ID NO: 5, wherein X is W or F); and a LAG3 binder comprising: CDR1 comprising the amino acid sequence `GRTFSDYVMG` (SEQ ID NO: 65); CDR2 comprising the amino acid sequence `AISESGGRTH` (SEQ ID NO: 66); and CDR3 comprising the amino acid sequence `TLLWWTSEYAPIKANDYDY` (SEQ ID NO: 67); and, optionally, a half-life extender.

~~In another aspect, there is provided a multispecific binder comprising:~~

- ~~————— (a) an immunoglobulin single variable domain (ISVD) that binds to programmed cell death protein 1 (PD1) comprising: a CDR1 comprising the amino acid sequence `IHAMG` (SEQ ID NO: 3) or `GSIASIHAMG` (SEQ ID NO: 6); a CDR2 comprising the amino acid sequence `VITXSGGITYYADSVKG` (SEQ ID NO: 4; wherein X is W or V) or `VITXSGGITY` (SEQ ID NO: 7; wherein X is W or V); and a CDR3 comprising the amino acid sequence `DKHQSSXYDY` (SEQ ID NO: 5, wherein X is W or F); and~~
- ~~————— (b) an immunoglobulin single variable domain that binds to lymphocyte activation gene 3 (LAG3) comprising: a CDR1 comprising the amino acid sequence `GRTFSDYVMG` (SEQ ID NO: 65) or `DYVMG` (amino acids 6-10 of SEQ ID NO: 65); a CDR2 comprising the amino acid sequence `AISESGGRTHYADSVKG` (SEQ ID NO: 66) or `AISESGGRTH` (amino acids 1-10 of SEQ ID NO: 66); and a CDR3 comprising the amino acid sequence `TLLWWTSEYAPIKANDYDY` (SEQ ID NO: 67); and,~~

~~—(c) a half-life extender and a C-terminal extender.~~

In an example, the PD1 binder comprises the amino acid sequence:

DVQLVESGGG VVQPGGSLRL SCAASGSIAS IHAMGWFRQA PGKEREFVAV ITWSGGITYY

ADSVKGRFTI SRDNSKNTVY LQMNSLRPED TALYYCAGDK HQSSWYDYWG QGTLVTVSS; and

5 (SEQ ID NO: 57); and the LAG3 binder comprises the amino acid sequence:

EVQLVE SGGGVVQPGG SLRLSCAASG RTFSDYVMGW FRQAPGKERE FVAAISESGG RTHYADSVKG

RFTISRDNK NTLYLQMNSL RPEDTALYYC ATTLLWWTSE YAPIKANDYD YWGQGTLVTV SS

(SEQ ID NO: 64); and, optionally, a half-life extender. In an example of the disclosure, the

PD1/LAG3 binder comprises the moieties, *e.g.*, in the order shown:

- 10
- the PD1 binder 102C12 (E1D,L11V,A14P,A74S,K83R,I89L) or 1PD102C12 (E1D, L11V, A14P, W52aV, N73X (*e.g.*, N73P or N73Q or N73S), A74S, K83R, I89L, W100aF);
 - a peptide linker such as 9GS, 20GS or 35 GS (*e.g.*,
GGGGSGGGSGGGSGGGSGGGSGGGSGGGSGGGSGGGGS (SEQ ID NO: 70));
- 15
- the LAG3 binder 11B09 or 11B09 (L11V,A14P,R41P,N43K,A62S,A74S,K83R,V89L);
 - a peptide linker such as 9GS, 20GS or 35 GS (*e.g.*,
GGGGSGGGSGGGSGGGSGGGSGGGSGGGSGGGSGGGGS (SEQ ID NO: 70));
 - a half-life extender such as ALB11002; and, optionally,

We claim:

~~1. A multispecific binder comprising:~~

~~(a) an immunoglobulin single variable domain (ISVD) that binds to programmed cell death protein 1 (PD1) comprising~~

~~a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 3 or SEQ ID NO: 6; a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 4 wherein X is W or V or SEQ ID NO: 7 wherein X is W or V; and~~

~~a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 5 wherein X is W or F; and~~

~~(b) an ISVD that binds to lymphocyte activation gene 3 (LAG3) comprising:~~

~~a CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 65 or amino acids 6-10 of SEQ ID NO: 65; a CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 66 or amino acids 1-10 of SEQ ID NO: 66; and a CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 67.~~

~~2. The multispecific binder of claim 1, wherein the ISVD that binds to PD1 comprises the amino acid sequence set forth in SEQ ID NO: 1 or 2 wherein the sequence comprises a mutation at residue 11 and/or 89 and optionally a substitution of the Asp at position 1 with a Glu; wherein said residue numbers are Kabat residue numbers.~~

31. A multispecific binder comprising an immunoglobulin single variable domain (ISVD) that binds PD1 and an ISVD that binds LAG3~~The multispecific binder of claim 1,~~ wherein the

ISVD that binds to PD1 comprises the amino acid sequence:

DVQLVESGGG-VVQPGGSLRL-SCAASGSIAS-IHAMGWFRQA-PGKEREFVAV-ITWSGGITYY

ADSVKGRFTI-SRDNSKNTVY-LQMNSLRPED-TALYYCAGDK-HQSSWYDYWG-QGTLVTVSS

(SEQ ID NO: 57,~~or said sequence optionally comprising a D1E mutation~~)or said sequence optionally comprising a D1E mutation;

EVQLVESGGGLVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDNKNT
VYLQMNSLRPEDTAIYYCAGDKHQSSWYDYWGQGTLVTVSS

(SEQ ID NO: 98,~~or said sequence optionally comprising a E1D mutation~~)or said sequence optionally comprising a E1D mutation;

EVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSSGGITYYADSVKGRFTISRDN SKNT
VYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGT LVTVSS

(SEQ ID NO: 99, ~~or said sequence optionally comprising a E1D mutation~~) or said sequence optionally comprising a E1D mutation;

5 DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSSGGITYYADSVKGRFTISRDN SKNT
VYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGT LVTVSS

(SEQ ID NO: 103, ~~or said sequence optionally comprising a D1E and/or N73S mutation~~) or said sequence optionally comprising a D1E and/or N73S mutation;

10 DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR DQSKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS

(SEQ ID NO: 104, ~~or said sequence optionally comprising a D1E mutation~~) or said sequence optionally comprising a D1E mutation; or

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR DPSKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS

15 (SEQ ID NO: 105, ~~or said sequence optionally comprising a D1E mutation~~) or said sequence optionally comprising a D1E mutation; or

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR DPSKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS (amino acids 1-119 of SEQ ID NO: 113, ~~or~~

20 ~~said sequence optionally comprising a D1E mutation~~) or said sequence optionally comprising a D1E mutation; or

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR DQSKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS (amino acids 1-119 of SEQ ID NO: 117, ~~or~~
~~said sequence optionally comprising a D1E mutation~~) or said sequence optionally comprising a D1E mutation; or

25 DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR DSSKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS (amino acids 1-119 of SEQ ID NO: 121, ~~or~~
~~said sequence optionally comprising a D1E mutation~~) or said sequence optionally comprising a D1E mutation.

30 42. The multispecific binder of claim 1, wherein the ISVD that binds LAG3 comprises the amino acid sequence set forth in SEQ ID NO: 64 or SEQ ID NO: 64 comprising a substitution of the Asp at position 1 with a Glu.

53. The multispecific binder of claim 1, wherein the multispecific binder further includes an ISVD that binds to human serum albumin comprising CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 60 or amino acids 1-5 of SEQ ID NO: 60; CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 61 or amino acids 1-10 of SEQ ID NO: 61; and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 62.

6. ~~A multispecific binder comprising:~~

~~(a) an immunoglobulin single variable domain (ISVD) that binds to programmed cell death protein 1 (PD1) comprising: a CDR1 comprising the amino acid sequence ~~IHAMG~~ (SEQ ID NO: 3) or ~~GSIASIHAMG~~ (SEQ ID NO: 6); a CDR2 comprising the amino acid sequence ~~VITXSGGITYYADSVKG~~ (SEQ ID NO: 4; wherein X is W or V) or ~~VITXSGGITY~~ (SEQ ID NO: 7; wherein X is W or V); and a CDR3 comprising the amino acid sequence ~~DKHQSSXYDY~~ (SEQ ID NO: 5, wherein X is W or F); and~~

~~(b) an immunoglobulin single variable domain that binds to lymphocyte activation gene 3 (LAG3) comprising: a CDR1 comprising the amino acid sequence ~~GRTFSDYVMG~~ (SEQ ID NO: 65) or ~~DYVMG~~ (amino acids 6-10 of SEQ ID NO: 65); a CDR2 comprising the amino acid sequence ~~AISESGGRTHYADSVKG~~ (SEQ ID NO: 66) or ~~AISESGGRTH~~ (amino acids 1-10 of SEQ ID NO: 66); and a CDR3 comprising the amino acid sequence ~~TLLWWTSEYAPIKANDYDY~~ (SEQ ID NO: 67); and,~~

~~(c) a half life extender and a C-terminal extender.~~

74. ~~The A~~ multispecific binder comprising an ISVD that binds PD1 and an ISVD that binds LAG3 of claim 6, wherein

(a) the ISVD ~~immunoglobulin single variable domain~~ that binds to PD1 comprises the amino acid sequence

DVQLVESGGG VVQPGGSLRL SCAASGSIAS IHAMGWFRQA PGKEREFAV ITWSSGITYY
ADSVKGRFTI SRDNSKNTVY LQMNSLRPED TALYYCAGDK HQSSWYDYG QGTLTVSS
(SEQ ID NO: 57);

EVQLVESGGGLVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFAVITWSSGITYYADSVKGRFTISRDNSKNT
VYLQMNSLRPEDTAIYYCAGDKHQSSWYDYGQGTLTVSS
(SEQ ID NO: 98);

EVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSSGGITYYADSVKGRFTISRDN SKNT
VYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGTLLTVSS

(SEQ ID NO: 99);

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSSGGITYYADSVKGRFTISRDN SKNT
5 VYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGTLLTVSS

(amino acids 1-119 of SEQ ID NO: 101);

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISRDN SKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGTLLTVSS

(SEQ ID NO: 103);

10 DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISRDN SKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGTLLTVSS

(SEQ ID NO: 104); or

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISRDN SKNT
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGTLLTVSS

15 (SEQ ID NO: 105); and,

(b) the ISVD immunoglobulin single variable domain that binds to LAG3

comprises the amino acid sequence

EVQLVE SGGGVVQPGG SLRLSCAASG RTFSDYVMGW FRQAPGKERE FVAAISESGG RTHYADSVKG
RFTISRDN SK NTLYLQMNSL RPEDTALYYC ATTLLWWTSE YAPIKANDYD YWGQGTLLTV SS

20 (SEQ ID NO: 64); or

DVQLVESGGGVVQPGGSLRLSCAASGR TFSYDYVMGWFRQAPGKEREFVAAISESGGRTHYADSVKGRFTISRDN SKNT
LYLQMNSLRPEDTALYYCATLLWWTSEYAPIKANDYDYWGQGTLLTVSS

(amino acids 1-128 of SEQ ID NO: 96).

25 85. The multispecific binder of claim 64, wherein the C-terminal extender is an alanine.

96. ~~The A~~ multispecific binder that binds PD1 and LAG3 comprising of any one of claim 6,
~~wherein the multispecific binder comprises:~~

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 98;
- 30 • a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 98;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 63;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;

- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 63;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a human serum albumin (HSA) ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and

5 • a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 99;

10 • a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;

- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;

15 • a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and

- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 20 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 99;

20 • a 20 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;

- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 20 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;

25 • a 20 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;

- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;

30 • a 9 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 99;
- a 9 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- 5 • a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9 GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- 10 • a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- 15 • a C-terminal Alanine;

or

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- a 20GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- 20 • a 20GS linker comprising the amino acid sequence set forth in SEQ ID NO: 100;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 57;
- 25 • a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

30 or

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105;
 - a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
 - a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105 (wherein the Asp at position 1 is replaced with a Glu);
- 5 • a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
 - a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
 - a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
 - a C-terminal Alanine;
- 10 or,
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105;
 - a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
 - a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105 (wherein the Asp at position 1 is substituted with a Glu);
- 15 • a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
 - a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
 - a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
 - a C-terminal Alanine;
- 20 or
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105;
 - a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
 - a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
 - a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- 25 • a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;
- or,
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 105;
 - a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- 30 • a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;

- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- 5
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104;
 - a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
 - a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104 (wherein the Asp at position 1 is replaced with a Glu);
 - a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- 10
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
 - a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
 - a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
 - a C-terminal Alanine;

or,

- 15
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104;
 - a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
 - a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104 (wherein the Asp at position 1 is replaced with a Glu);
 - a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- 20
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
 - a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
 - a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
 - a C-terminal Alanine;

or,

- 25
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104;
 - a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
 - a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
 - a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
 - a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- 30
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 104;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine

or

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asn at position 73 is replaced with Ser);
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asp at position 1 is replaced with Glu and the Asn at position 73 is replaced with Ser);
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asn at position 73 is replaced with Ser);
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asp at position 1 is replaced with Glu and the Asn at position 73 is replaced with Ser);
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asn at position 73 is replaced with Ser);
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine;

or,

- a PD1 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 103 (wherein the Asn at position 73 is replaced with Ser);
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a LAG3 ISVD comprising the amino acid sequence set forth in SEQ ID NO: 64;
- a 9GS linker comprising the amino acid sequence set forth in SEQ ID NO: 125;
- a HSA ISVD comprising the amino acid sequence set forth in SEQ ID NO: 59; and
- a C-terminal Alanine

wherein said residue numbers are Kabat residue numbers.

~~107.~~ The multispecific binder of claim 6, wherein the multispecific binder comprises the amino acid sequence set forth in SEQ ID NO: 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123 or 124.

~~11. The multispecific binder of claim 6, wherein the multispecific binder binds to PD1 and LAG3.~~

~~12. The multispecific binder of claim 6, wherein the half-life extender is a human serum albumin-ISVD that binds to human serum albumin comprising:~~

~~CDR1 comprising the amino acid sequence GFTFSFGMS (SEQ ID NO: 60) or SFGMS (amino acids 1-5 of SEQ ID NO: 60);~~

~~CDR2 comprising the amino acid sequence SISGSGSDTLYADSVKG (SEQ ID NO: 61) or~~

~~SISGSGSDTL (amino acids 1-10 of SEQ ID NO: 61); and~~

~~CDR3 comprising the amino acid sequence GGSLSR (SEQ ID NO: 62).~~

~~13. The multispecific binder of claim 12 wherein the ISVD that binds human serum albumin comprises the amino acid sequence~~

~~EVQLVESGGG VVQPGNSLR LSCAASGFTFS SFCMSWVRQA PGKGLEWVSS ISGSGSDTLYADSVKGRFTI
SRDNAKTTLY LQMNSLRPED TALYYCTIGG SLRSSQCTL VTVSSA
(SEQ ID NO: 59).~~

~~14. A multispecific binder that cross-blocks a multispecific binder of claim 6 from binding to
LAG3 or PD1 and LAG3.~~

~~158.~~ An injection device or vessel that comprises the multispecific binder of any one of claims 64 to 6, optionally in association with a further therapeutic agent.

~~169.~~ A composition comprising a multispecific binder of any one of claims 4 to 6 and at least one pharmaceutically acceptable carrier, diluent or excipient.

~~1710.~~ The composition of claim ~~169~~, wherein the multispecific binder comprises the amino acid sequence set forth in SEQ ID NO: 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, or 124.

~~1811.~~ The composition of claim ~~1710~~, wherein the multispecific binder comprises the amino acid sequence set forth in SEQ ID NO:110.

~~1249.~~ A multispecific binder consisting of the amino acid set forth in SEQ ID NO: 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, or 124.

~~2013.~~ A composition comprising the multispecific binder of claim ~~1912~~ and at least one pharmaceutically acceptable carrier, diluent or excipient.

~~2414.~~ A multispecific binder consisting of the amino acid set forth in SEQ ID NO: 110.

2215. A composition comprising the multispecific binder of claim 2114 and at least one pharmaceutically acceptable carrier, diluent or excipient.

2316. A multispecific binder comprising a programmed cell death protein 1 (PD1) binder having the amino acid sequence set forth in SEQ ID NO: 57 and a lymphocyte activation gene 3 (LAG3) binder having the amino acid sequence set forth in SEQ ID NO: 64.

2417. The multispecific binder of claim 1623, wherein the multispecific binder further comprises a human serum albumin (HSA) binder having the amino acid sequence set forth in SEQ ID NO: 59.

2518. A multispecific binder comprising an N-terminal immunoglobulin single variable domain (ISVD) that binds programmed cell death protein 1 (PD1) comprising the amino acid sequence set forth in SEQ ID NO: 57; an ISVD that binds lymphocyte activation gene 3 (LAG3) comprising the amino acid sequence set forth in SEQ ID NO: 64; an ISVD that binds human serum albumin (HSA) comprising the amino acid sequence set forth in SEQ ID NO: 59; and a C-terminal Alanine.

2619. A multispecific binder comprising an N-terminal immunoglobulin single variable domain (ISVD) that binds programmed cell death protein 1 (PD1) comprising the amino acid sequence set forth in SEQ ID NO: 57; a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58; an ISVD that binds lymphocyte activation gene 3 (LAG3) comprising the amino acid sequence set forth in SEQ ID NO: 64; a 35GS linker comprising the amino acid sequence set forth in SEQ ID NO: 58; an ISVD that binds human serum albumin (HSA) comprising the amino acid sequence set forth in SEQ ID NO: 59; and a C-terminal Alanine.

2720. A composition comprising the multispecific binder of claim 2417 and at least one pharmaceutically acceptable carrier, diluent or excipient.

2821. A multispecific binder comprising the amino acid set forth in SEQ ID NO: 110.