

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  
5 SGGGVVQPGG SLRLSCAASG RTFSDYVMGW FRQAPGKERE FVA AISESGG RTHYADSVKG RFTISRDN SK  
NTLYLQMNSL RPEDTALYYC ATLLWWTSE YAPIKANDYD YWGQGLTVTV SS (SEQ ID NO: 64).

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  
10 that binds to PD1 comprises the amino acid sequence:

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYY

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

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

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

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSSGGITYYADSVKGRFTISRDN SKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSWYDYGQGTTLVTVSS (SEQ ID NO: 103) or said sequence

optionally comprising a D1E and/or N73S mutation;

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR DQSKNT

5 VYLQMNSLRPEDTALYYCAGDKHQSSFYDYGQGTTLVTVSS(SEQ ID NO: 104) or said sequence

optionally comprising a D1E mutation;

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR DPSKNT

VYLQMNSLRPEDTALYYCAGDKHQSSFYDYGQGTTLVTVSS(SEQ ID NO: 105) or said sequence

optionally comprising a D1E mutation;

10 DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR DPSKNT

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

said sequence optionally comprising a D1E mutation;

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR DQSKNT

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

15 said sequence optionally comprising a D1E mutation; or

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSSGGITYYADSVKGRFTISR

DSSKNTVYLQMNSLRPEDTALYYCAGDKHQSSFYDYGQGTTLVTVSS (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 PD1

20 and an ISVD that binds LAG3 wherein

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

DVQLVESGGG VVQPGGSLRL SCAASGSIAS IHAMGWFRQA PGKEREFVAV ITWSSGGITYY  
ADSVKGRFTI SRDN SKNTVY LQMNSLRPED TALYYCAGDK HQSSWYDYG QGTTLVTVSS

(SEQ ID NO: 57);

25 EVQLVESGGGLVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSSGGITYYADSVKGRFTISRDN SKNT

VYLQMNSLRPEDTAIYYCAGDKHQSSWYDYGQGTTLVTVSS

(SEQ ID NO: 98);

EVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSSGGITYYADSVKGRFTISRDN SKNT

VYLQMNSLRPEDTALYYCAGDKHQSSWYDYGQGTTLVTVSS

30 (SEQ ID NO: 99);

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSSGGITYYADSVKGRFTISRDN SKNT

VYLQMNSLRPEDTALYYCAGDKHQSSWYDYGQGTTLVTVSS

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

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKERE FVAVITVSGGITYYADSVKGRFTISRDN SKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS

(SEQ ID NO: 103);

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKERE FVAVITVSGGITYYADSVKGRFTISR DQSKNT  
5 VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS

(SEQ ID NO: 104); or

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKERE FVAVITVSGGITYYADSVKGRFTISR DPSKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS

(SEQ ID NO: 105); and,

10 (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 TFSYVMGWFRQAPGKERE FVAAISESGGRTHYADSVKGRFTISR DN SKNT  
15 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;
- 20 • 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;
- 25 • 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,

- 30 • 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;
- 5     • 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;
- 10     • 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;
- 15     • 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,

- 20     • 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;
- 25     • 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;

30     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;
- 5 • 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;
- 10 • 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,

- 15 • 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
- 20 • 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
- 25 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
- 30 • 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;
- 5 • 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,  
 10 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  
 15 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 an example, the PD1 binder comprises the amino acid sequence:

DVQLVESGGG VVQPGGSLRL SCAASGSIAS IHAMGWFRQA PGKEREFVAV ITWSGGITYY

ADSVKGRFTI SRDNSKNTVY LQMNSLRPED TALYYCAGDK HQSSWYDYWG QGTLTVTVSS; 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 YWGQGTLLTVV 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 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:

- 5 DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYY  
ADSVKGRFTISRDN SKNTVYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGT LVTVSS (SEQ ID NO: 57) or  
said sequence optionally comprising a D1E mutation;  
EVQLVESGGGLVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDN SKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGT LVTVSS (SEQ ID NO: 98) or said sequence optionally  
10 comprising a E1D mutation;  
EVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDN SKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGT LVTVSS (SEQ ID NO: 99) or said sequence optionally  
comprising a E1D mutation;  
DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITWSGGITYYADSVKGRFTISRDN SKNT  
15 VYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGT LVTVSS (SEQ ID NO: 103) or said sequence  
optionally comprising a D1E and/or N73S mutation;  
DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DQSKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS (SEQ ID NO: 104) or said sequence  
optionally comprising a D1E mutation;  
20 DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DPSKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS (SEQ ID NO: 105) or said sequence  
optionally comprising a D1E mutation;  
DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DPSKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS (amino acids 1-119 of SEQ ID NO: 113) or  
25 said sequence optionally comprising a D1E mutation;  
DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DQSKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS (amino acids 1-119 of SEQ ID NO: 117) or  
said sequence optionally comprising a D1E mutation; or  
DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFVAVITVSGGITYYADSVKGRFTISR DSSKNT  
30 VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGT LVTVSS (amino acids 1-119 of SEQ ID NO: 121) or  
said sequence optionally comprising a D1E mutation.

2. 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.

3. 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.

4. A multispecific binder comprising an ISVD that binds PD1 and an ISVD that binds LAG3 wherein

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

DVQLVESGGG VVQPGGSLRL SCAASGSIAS IHAMGWFRQA PGKEREFAV ITWSGGITYY

ADSVKGRFTI SRDNSKNTVY LQMNSLRPED TALYYCAGDK HQSSWYDYWG QGTLVTVSS

(SEQ ID NO: 57);

EVQLVESGGGLVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFAVITWSGGITYYADSVKGRFTISRDNKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGTLVTVSS

(SEQ ID NO: 98);

EVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFAVITWSGGITYYADSVKGRFTISRDNKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSWYDYWGQGTLVTVSS

(SEQ ID NO: 99);

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFAVITWSGGITYYADSVKGRFTISRDNKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGTLVTVSS

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

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFAVITVSGGITYYADSVKGRFTISRDNKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGTLVTVSS

(SEQ ID NO: 103);

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFAVITVSGGITYYADSVKGRFTISRDSKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGTLVTVSS

(SEQ ID NO: 104); or

DVQLVESGGGVVQPGGSLRLSCAASGSIASIHAMGWFRQAPGKEREFAVITVSGGITYYADSVKGRFTISRDPKNT  
VYLQMNSLRPEDTALYYCAGDKHQSSFYDYWGQGTLVTVSS

(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 ATLLWWTSE YAPIKANDYD YWGQGTLLTV SS

(SEQ ID NO: 64); or

5 DVQLVESGGGVVQPGGSLRLSCAASGRTFSDYVMGWFRQAPGKEREFVAAISESGGRTHYADSVKGRFTISRDN SKNT  
LYLQMNSLRPEDTALYYCATLLWWTSEYAPIKANDYDYWGQGTLLTVSS

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

5. The multispecific binder of claim 4, wherein the C-terminal extender is an alanine.

10

6. 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;
- 15 • 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;
- 20 • 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;
- 25 • 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;
- 30 • 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;
- 5 • 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;
- 10 • 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,

- 15 • 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;
- 20 • 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;

25 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;
- 30 • 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;
- 5 • 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,

- 10 • 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
- 15 • 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
- 20 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
- 25 • 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
- 30 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
  - 5     • 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;
  - 10     • 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;
  - 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: 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);
  - 25     • 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;
- 30     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);
- 5      • 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;
- 10    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;
- 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: 104;
  - 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: 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);
- 30      • 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: 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.

7. The multispecific binder of claim 6, wherein the multispecific binder comprises the amino  
5 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.

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

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

10. The composition of claim 9, wherein the multispecific binder comprises the amino acid  
15 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 composition of claim 10, wherein the multispecific binder comprises the amino acid  
sequence set forth in SEQ ID NO:110.

20 12. 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.

13. A composition comprising the multispecific binder of claim 12 and at least one  
25 pharmaceutically acceptable carrier, diluent or excipient.

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

15. A composition comprising the multispecific binder of claim 14 and at least one  
30 pharmaceutically acceptable carrier, diluent or excipient.

16. 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.
- 5 17. The multispecific binder of claim 16, wherein the multispecific binder further comprises a human serum albumin (HSA) binder having the amino acid sequence set forth in SEQ ID NO: 59.
18. 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  
10 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.
- 15 19. 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  
20 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.
20. A composition comprising the multispecific binder of claim 17 and at least one pharmaceutically acceptable carrier, diluent or excipient.
- 25 21. A multispecific binder comprising the amino acid set forth in SEQ ID NO: 110.