

CLAIMS

What is claimed is:

1. An antibody, or an antigen-binding fragment thereof, that is capable of binding to a neuraminidase (NA) from:
 - (i) an influenza A virus (IAV), wherein the IAV comprises a Group 1 IAV, a Group 2 IAV, or both; and
 - (ii) an influenza B virus (IBV).
2. The antibody or antigen-binding fragment of claim 1, comprising a heavy chain variable domain (VH) comprising a complementarity determining region (CDR)H1, a CDRH2, and a CDRH3, and a light chain variable domain (VL) comprising a CDRL1, a CDRL2, and a CDRL3, wherein:
 - (i) optionally, the CDRH1 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.: 147, 3, 15, 27, 39, 51, 63, 75, 87, 99, 111, 123, 135, 159, and 231, or a functional variant thereof comprising one, two, or three acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline-encoded amino acid;
 - (ii) optionally, the CDRH2 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.: 148, 4, 16, 28, 40, 52, 64, 76, 88, 100, 112, 124, 136, 160, and 232, or a functional variant thereof comprising one, two, or three amino acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline-encoded amino acid;
 - (iii) the CDRH3 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.: 149, 5, 17, 29, 172, 41, 53, 65, 77, 89, 184, 101, 113, 125, 137, 161, and 233, or a functional variant thereof comprising one, two, or three amino acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline-encoded amino acid;
 - (iv) optionally, the CDRL1 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.: 153, 9, 21, 33, 45, 57, 69, 81, 93, 105, 117, 129,

141, 165, and 234, or a functional variant thereof comprising one, two, or three amino acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline-encoded amino acid;

(v) optionally, the CDRL2 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.: 154, 10, 22, 34, 46, 58, 70, 82, 94, 106, 118, 130, 142, 166, and 235, or a functional variant thereof comprising one, two, or three amino acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline-encoded amino acid; and/or

(vi) optionally, the CDRL3 comprises or consists of the amino acid sequence set forth in any one of SEQ ID NOs.: 155, 11, 23, 35, 175, 178, 181, 47, 59, 71, 83, 95, 187, 193, 107, 119, 131, 143, 190, 167, and 236, or a functional variant thereof comprising having one, two, or three amino acid substitutions, one or more of which substitutions is optionally a conservative substitution and/or is a substitution to a germline-encoded amino acid.

3. The antibody or antigen-binding fragment of claim 2, wherein:

(i) the VH comprises or consists of an amino acid sequence having at least 80% (*e.g.*, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more) identity to the amino acid sequence set forth in any one of SEQ ID NOs.: 199, 2, 14, 26, 171, 38, 50, 62, 74, 86, 183, 98, 110, 122, 134, 146, 158, 203, 207, 216, and 228, wherein sequence variation is optionally limited to one or more framework regions and/or sequence variation comprises one or more substitution to a germline-encoded amino acid; and/or

(ii) the VL comprises or consists of an amino acid sequence having at least 80% (*e.g.*, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or more) identity to the amino acid sequence set forth in any one of SEQ ID NOs.: 201, 8, 20, 32, 44, 56, 68, 80, 92, 104, 116, 128, 140, 152, 174, 177, 180, 186, 189, 192, 164, 205, 209, 217, and 230, wherein sequence variation is optionally limited to one or more framework regions and/or sequence variation comprises one or more substitution to a germline-encoded amino acid.

4. A polypeptide comprising an amino acid sequence according to SEQ ID NO.:219, wherein the polypeptide is capable of binding to an influenza virus neuraminidase (NA).

5. The polypeptide of claim 4, wherein the polypeptide comprises an antibody heavy chain variable domain (VH), or a fragment thereof, and the amino acid sequence according to SEQ ID NO.:219 is optionally comprised in the VH or fragment thereof.

6. The polypeptide of claim 4 or 5, wherein the amino acid sequence according to SEQ ID NO.:219 comprises any one of SEQ ID NOs.: 149, 5, 17, 29, 172, 41, 53, 65, 77, 89, 184, 101, 113, 125, 137, and 161.

7. The polypeptide of any one of claims 4-6, wherein the polypeptide or VH further comprises:

- (i) an amino acid sequence according to SEQ ID NO.:220; and/or
- (ii) an amino acid sequence according to SEQ ID NO.:221.

8. The polypeptide of any one of claims 4-7, further comprising an antibody light chain variable domain (VL), wherein, optionally, the VL comprises:

- (i) an amino acid sequence according to SEQ ID NO.:222;
- (ii) an amino acid sequence according to SEQ ID NO.:223; and/or
- (iii) an amino acid sequence according to SEQ ID NO.:224.

9. The polypeptide of any one of claims 5-8, wherein the VH comprises or consists of an amino acid sequence having at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% identity to the amino acid sequence of any one of SEQ ID NOs.: 199, 2, 14, 26, 171, 38, 50, 62, 74, 86, 183, 98, 110, 122, 134, 146, 158, 203, 207, 216, and 228.

10. The polypeptide of claim 8 or 9, wherein the VL comprises or consists of an amino acid sequence having at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% identity to the amino acid sequence of any one of SEQ ID NOs.: 201, 8, 20, 32, 44, 56, 68, 80, 92, 104, 116, 128, 140, 152, 174, 177, 180, 186, 189, 192, 164, 205, 209, 217, and 230.

11. The polypeptide of any one of claims 4-10, wherein the polypeptide comprises an antibody or an antigen-binding fragment thereof.

12. An antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) amino acid sequence and a light chain variable domain (VL) amino acid sequence, wherein the VH comprises or consists of an amino acid sequence having at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% identity to the amino acid sequence of any one of SEQ ID NOs.: 199, 2, 14, 26, 171, 38, 50, 62, 74, 86, 183, 98, 110, 122, 134, 146, 158, 203, 207, 216, and 228, and wherein the VL comprises or consists of an amino acid sequence having at least 90%, at least 92%, at least 95%, at least 97%, or at least 99% identity to the amino acid sequence of any one of SEQ ID NOs.: 201, 8, 20, 32, 44, 56, 68, 80, 92, 104, 116, 128, 140, 152, 174, 177, 180, 186, 189, 192, 164, 205, 209, 217, and 230,

wherein the antibody or antigen-binding fragment thereof is capable of binding to a neuraminidase (NA) from: (i) an influenza A virus (IAV), wherein the IAV comprises a Group 1 IAV, a Group 2 IAV, or both; and/or (ii) an influenza B virus (IBV).

13. The polypeptide of any one of claims 4-11 or the antibody or antigen-binding fragment of claim 12, which is capable of binding to a neuraminidase (NA) from: (i) an influenza A virus (IAV), wherein the IAV comprises a Group 1 IAV, a Group 2 IAV, or both; and/or (ii) an influenza B virus (IBV), and wherein, optionally, the antibody or antigen-binding fragment is capable of (1) inhibiting NA sialidase activity and/or (2) neutralizing infection by the IAV and/or IBV.

14. The antibody or antigen-binding fragment of any one of claims 1-3, 12 and 13, or the polypeptide of claim 11, which is a IgG, IgA, IgM, IgE, or IgD isotype.

15. The antibody or antigen-binding fragment of any one of claims 1-3 and 12-14, or the polypeptide of claim 11, which is an IgG isotype selected from IgG1, IgG2, IgG3, and IgG4.

16. The antibody or antigen-binding fragment of any one of claims 1-3 and 12-15, or the polypeptide of claim 11, wherein the antibody, or the antigen-binding fragment, comprises a human antibody, a monoclonal antibody, a purified antibody, a single chain antibody, a Fab, a Fab', a F(ab')₂, or Fv.

17. The antibody or antigen-binding fragment of any one of claims 1-3 and 12-16, or the polypeptide of claim 11, wherein the antibody or antigen-binding fragment is a multi-specific antibody or antigen-binding fragment.

18. The antibody or antigen-binding fragment of any one of claims 1-3 and 12-17, or the polypeptide of claim 11, wherein the antibody or antigen-binding fragment comprises an (*e.g.*, IgG1) Fc polypeptide or a fragment thereof.

19. The antibody or antigen-binding fragment of claim 18, or the polypeptide of claim 18, wherein the Fc polypeptide or fragment thereof comprises:

(i) a mutation that increases binding affinity to a human FcRn (*e.g.*, as measured using surface plasmon resonance (SPR) (*e.g.*, Biacore, *e.g.*, T200 instrument, using manufacturer's protocols)), as compared to a reference Fc polypeptide that does not comprise the mutation; and/or

(ii) a mutation that increases binding affinity to a human FcγR (*e.g.*, as measured using surface plasmon resonance (SPR) (*e.g.*, Biacore, *e.g.*, T200 instrument, using manufacturer's protocols)) as compared to a reference Fc polypeptide that does not comprise the mutation.

20. The antibody or antigen-binding fragment of claim 19, or the polypeptide of claim 19, wherein the mutation that increases binding affinity to a human FcRn comprises:

- (1) M428L; N434S; N434H; N434A; N434S; M252Y; S254T; T256E; T250Q; P257I; Q311I; D376V; T307A; E380A; or any combination thereof; and/or
- (2) S239D; I332E; A330L; G236A; or any combination thereof.

21. An isolated polynucleotide encoding the antibody or antigen-binding fragment of any one of claims 1-3 and 12-20, or encoding a VH, a heavy chain, a VL, and/or a light chain of the antibody or the antigen-binding fragment.

22. An isolated polynucleotide encoding the polypeptide of any one of claims 4-11 and 13-20.

23. The polynucleotide of claim 21 or 22, wherein (1) the polynucleotide comprises deoxyribonucleic acid (DNA) or ribonucleic acid (RNA), wherein the RNA optionally comprises messenger RNA (mRNA); and/or

(2) the polynucleotide comprises a modified nucleoside, a cap-1 structure, a cap-2 structure, or any combination thereof, wherein, optionally,

the polynucleotide comprises a pseudouridine, a N6-methyladenosine, a 5-methylcytidine, a 2-thiouridine, or any combination thereof, wherein, further optionally,

the pseudouridine comprises N1-methylpseudouridine.

24. The polynucleotide of any one of claims 21-23, comprising a polynucleotide having at least 50% (*e.g.*, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 94%, 94%, 95%, 96%, 97%, 98%, 99%, or more) identity to the

polynucleotide sequence set forth in any one or more of SEQ ID NOs.: 198, 200, 1, 13, 25, 170, 37, 49, 61, 73, 85, 182, 97, 109, 121, 133, 145, 157, 6, 18, 30, 42, 54, 66, 78, 90, 102, 114, 126, 138, 150, 162, 7, 19, 31, 173, 176, 179, 43, 55, 67, 79, 91, 185, 188, 191, 103, 115, 127, 139, 151, 163, 12, 24, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 202, 206, 204, 208, 227, and 229.

25. A recombinant vector comprising the polynucleotide of any one of claims 21-24.

26. A host cell comprising the polynucleotide of any one of claims 21-24 and/or the vector of claim 25, wherein the polynucleotide is optionally heterologous to the host cell and/or wherein the host cell is capable of expressing the encoded antibody or antigen-binding fragment or polypeptide.

27. An isolated human B cell comprising the polynucleotide of any one of claims 21-24 and/or the vector of claim 25, wherein polynucleotide is optionally heterologous to the human B cell and/or wherein the human B cell is immortalized.

28. A composition comprising:

- (i) the antibody or antigen-binding fragment of any one of claims 1-3 and 12-20;
 - (ii) the polypeptide of any one of claims 4-11 and 13-20;
 - (iii) the polynucleotide of any one of claims 21-24;
 - (iv) the recombinant vector of claim 25;
 - (v) the host cell of claim 26; and/or
 - (vi) the human B cell of claim 27,
- and a pharmaceutically acceptable excipient, carrier, or diluent.

29. A composition comprising the polynucleotide of any one of claims 21-24 or the vector of claim 25 encapsulated in a carrier molecule, wherein the carrier

molecule optionally comprises a lipid, a lipid-derived delivery vehicle, such as a liposome, a solid lipid nanoparticle, an oily suspension, a submicron lipid emulsion, a lipid microbubble, an inverse lipid micelle, a cochlear liposome, a lipid microtubule, a lipid microcylinder, lipid nanoparticle (LNP), or a nanoscale platform.

30. A method of making an antibody or antigen-binding fragment of any one of claims 1-3 and 12-20, comprising culturing the host cell of claim 26 or the human B cell of claim 27 for a time and under conditions sufficient for the host cell or human B cell, respectively, to express the antibody or antigen-binding fragment, wherein, optionally, the method further comprises

isolating the antibody or antigen-binding fragment.

31. Use of the antibody or antigen-binding fragment of any one of claims 1-3 and 12-20, the polypeptide of any one of claims 4-11 and 13-20, the polynucleotide of any one of claims 21-24, the recombinant vector of claim 25, the host cell of claim 26, the human B cell of claim 27, and/or the composition of claim 28 or 29, in the preparation of a medicament for the treatment or prevention of an IAV infection and/or an IBV infection in a subject.

32. A method for *in vitro* diagnosis of an IAV infection and/or an IBV infection, the method comprising:

- (i) contacting a sample from a subject with an antibody or antigen-binding fragment of any one of claims 1-3 and 12-20; and
- (ii) detecting a complex comprising an antigen and the antibody, or comprising an antigen and the antigen-binding fragment.

33. Use according to claim 31, wherein:

(i) the IAV comprises a Group 1 IAV, a Group 2 IAV, or both, wherein, optionally, the Group 1 IAV NA comprises a N1, a N4, a N5, and/or a N8; and/or the Group 2 IAV NA comprises a N2, a N3, a N6, a N7, and/or a N9, wherein, further optionally, the N1 is from A/California/07/2009, is from A/California/07/2009 I223R/H275Y, is from A/Swine/Jiangsu/J004/2018, is from A/Stockholm/18/2007, is from A/Brisbane/02/2018, is from A/Michigan/45/2015, is from A/Mississippi/3/2001, is from A/Netherlands/603/2009, is from A/Netherlands/602/2009, is from A/Vietnam/1203/2004, is from A/G4/SW/Shangdong/1207/2016, is from A/G4/SW/Henan/SN13/2018, is from A/G4/SW/Jiangsu/J004/2018, and/or is from A/New Jersey/8/1976; the N4 is from A/mallard duck/Netherlands/30/2011; the N5 is from A/aquatic bird/Korea/CN5/2009; the N8 is from A/harbor seal/New Hampshire/179629/2011; the N2 is from A/Washington/01/2007, is from A/HongKong/68, is from A/HongKong/2671/2019, is from A/South Australia/34/2019, is from A/Switzerland/8060/2017, is from A/Singapore/INFIMH-16-0019/2016, is from A/Switzerland/9715293/2013, is from A/Leningrad/134/17/57, is from A/Florida/4/2006, is from A/Netherlands/823/1992, is from A/Norway/466/2014, is from is from A/Texas/50/2012, is from A/Victoria/361/2011, is from A/SW/Mexico/SG1444/2011, is from A/Aichi/2/1968, is from A/Bilthoven/21793/1972, is from A/Netherlands/233/1982, is from A/Shanghai/11/1987, is from A/Nanchang/933/1995, is from A/Fukui/45/2004, A/Brisbane/10/2007, is from A/Tanzania/205/2010; the N3 is from A/Canada/rv504/2004; the N6 is from A/swine/Ontario/01911/1/99; the N7 is from A/Netherlands/078/03; and/or the N9 is from A/Anhui/2013, is from A/Hong Kong/56/2015; and/or

(ii) the IBV NA is from: B/Lee/10/1940 (Ancestral); B/Brisbane/60/2008 (Victoria); B/Malaysia/2506/2004 (Victoria); B/Malaysia/3120318925/2013 (Yamagata); B/Wisconsin/1/2010 (Yamagata); B/Yamanashi/166/1998 (Yamagata); B/Brisbane/33/2008 (Victoria); B/Colorado/06/2017 (Victoria); B/Hubei-wujiang/158/2009 (Yamagata); B/Massachusetts/02/2012 (Yamagata); B/Netherlands/234/2011; B/Perth/211/2001(Yamagata); B/Phuket/3073/2013

(Yamagata); B/Texas/06/2011 (Yamagata); B/HongKong/05/1972; B/Harbin/7/1994 (Victoria); B/Washington/02/2019 (Victoria); B/Perth/211/2011, or any combination thereof.