

CLAIMS:

1. Use of a bispecific antibody comprising:
 - (a) a first polypeptide subunit comprising a heavy chain variable region comprising a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 6, and a CDR3 sequence of SEQ ID NO: 13 in a human heavy chain framework;
 - (b) a second polypeptide subunit comprising a light chain variable region comprising a CDR1 sequence of SEQ ID NO: 49, a CDR2 sequence of SEQ ID NO: 50, and a CDR3 sequence of SEQ ID NO: 51, in a human light chain framework;
wherein the first polypeptide subunit and the second polypeptide subunit together have binding affinity to the first CD38 epitope; and
 - (c) a third polypeptide subunit comprising an antigen-binding domain of a heavy-chain antibody comprising a CDR1 sequence of SEQ ID NO: 3, a CDR2 sequence of SEQ ID NO: 9, and a CDR3 sequence of SEQ ID NO: 16 in a human heavy chain framework, in a monovalent or bivalent configuration;
wherein the third polypeptide subunit has binding affinity to the second, non-overlapping CD38 epitope in the manufacture of a medicament for treating a disease or disorder characterized by expression of CD38.
2. The use of claim 1, wherein the bispecific antibody further comprises an Fc region selected from the group consisting of: a human IgG1 Fc region, a human IgG4 Fc region, a silenced human IgG1 Fc region, and a silenced human IgG4 Fc region.
3. The use of claim 1, wherein the bispecific antibody comprises an asymmetric interface between a CH3 domain of the first polypeptide subunit and a CH3 domain of the third polypeptide subunit.
4. The use of claim 1, wherein the bispecific antibody comprises:
 - (a) a first heavy chain polypeptide comprising the sequence of SEQ ID NO: 46;
 - (b) a first light chain polypeptide comprising the sequence of SEQ ID NO: 48; and
 - (c) a second heavy chain polypeptide comprising the sequence of SEQ ID NO: 47.

5. The use of claim 1, wherein the disease or disorder is characterized by a hydrolase enzymatic activity of CD38, a cyclase enzymatic activity of CD38, or a combination thereof.
6. The use of claim 1, wherein the disease or disorder is a telomere shortening disease.
7. The use of claim 6, wherein the telomere shortening disease is selected from the group consisting of: accelerated aging, aplastic anemia, dyskeratosis congenita, Franconi's anemia, and idiopathic pulmonary fibrosis.
8. The use of claim 1, wherein the disease or disorder is an inflammatory disease.
9. The use of claim 8, wherein the inflammatory disease is selected from the group consisting of: ulcerative colitis, graft versus host disease (GvHD), acute GvHD, chronic GvHD, transplant-associated GvHD, and acute kidney injury.
10. The use of claim 1, wherein the disease or disorder is a fibrosis-associated disorder.
11. The use of claim 10, wherein the fibrosis-associated disorder is scleroderma.
12. The use of claim 1, wherein the disease or disorder is a metabolic syndrome.
13. The use of claim 12, wherein the metabolic syndrome is selected from the group consisting of: type II diabetes mellitus (T2DM), obesity, and systemic inflammation.
14. Use of a bispecific antibody comprising:
 - (a) a first heavy chain polypeptide comprising the sequence of SEQ ID NO: 46;
 - (b) a first light chain polypeptide comprising the sequence of SEQ ID NO: 48; and
 - (c) a second heavy chain polypeptide comprising the sequence of SEQ ID NO: 47in the manufacture of a medicament for treating a disease or disorder characterized by reduced sirtuin activity, wherein the bispecific antibody is to be administered to a subject with the disease or disorder.

15. The use of claim 14, wherein nicotinamide mononucleotide (NMN) is to be further administered to the subject.
16. The use of claim 14, wherein the disease or disorder is a metabolic disease or disorder.
17. The use of claim 14, wherein the disease or disorder is a cardiovascular disease or disorder.
18. The use of claim 14, wherein the disease or disorder is a neurodegenerative disease or disorder.
19. The use of claim 14, wherein the disease or disorder is a cancer.
20. The use of claim 14, wherein the bispecific antibody is to be administered to the subject as a pharmaceutical composition.