Tn3 scaffold comprises two CD40L-specific monomer subunits; wherein the Tn3 scaffold comprises SEQ ID NO: 1, and wherein the Tn3 scaffold is to be administered at a loading dose of 1500 mg about every 2 weeks for at least 3 doses, and wherein the Tn3 scaffold is to be administered at a maintenance dose of 1500 mg every 4 weeks.

**[0009]** Provided herein are methods of treating Sjögren's syndrome (SS) in a subject in need thereof comprising administering a Tn3 scaffold at a dose of about 1500 mg, about 2500 mg, or about 3000 mg to the subject, wherein the Tn3 scaffold comprises SEQ ID NO: 1.

In examples, at least one CD40L-specific monomer subunit is fused or conjugated to a polyethylene glycol (PEG) directly. In examples, at least one CD40L-specific monomer subunit is fused or conjugated to a polyethylene glycol (PEG) via a linker. In examples, the linker comprises a peptide linker. In examples, the linker comprises SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, or SEQ ID NO: 10. In examples, at least one CD40L-specific monomer subunit is fused or conjugated to an albumin. In examples, the albumin is human serum albumin (HSA). In examples, the HSA is a variant HSA comprising SEQ ID NO: 4.

**[0012]** Provided are methods of treating Sjögren's syndrome (SS) in a subject in need thereof. In examples, a method may comprise administering a Tn3 scaffold at a dose of about 1500 mg, about 2500 mg, or about 3000 mg to the subject of need. In examples, a method may comprise administering a Tn3 scaffold comprised of SEQ ID NO: 1. In examples, a Tn3 scaffold is administered as an induction dose and as one or more maintenance doses thereafter. In examples, an induction dose and maintenance doses are the same amount. In examples, an induction dose and maintenance doses are different amounts. In examples, least one dose is 3000 mg. In examples, an induction dose and at least one maintenance dose are administered about 1 month apart, about 2 months apart, about 3 months apart, about 4 months, or about 6 months apart. In examples, an induction dose comprises administering a Tn3 scaffold about every 2 weeks for at least 3 doses and the maintenance dose comprises administering a Tn3 scaffold once about every 4 weeks for at least 4 doses. In examples, a Tn3 scaffold comprises SEQ ID NO: 1. In examples, the method is effective in reducing a ESSDAI score as compared to an otherwise comparable method wherein the subject receives an equivalent administration. In examples, the reduction is of at least about 1 point, 2 points, 3 points, 4 points, or 5 points. In examples, the reduction is of at least about 6 points.

**[0012a]** In another aspect, the present disclosure refers to a use of a Tn3 scaffold comprising SEQ ID NO: 1 in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 scaffold is to be administered at a loading dose of 1500 mg about every 2 weeks for at least 3 doses, and wherein the Tn3 scaffold is to be administered at a maintenance dose of 1500 mg every 4 weeks.

**[0012b]** In yet another aspect, the present disclosure refers to a use of a Tn3 scaffold in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 comprises two CD40L-specific monomer subunits and a human serum albumin; wherein the Tn3 scaffold comprises SEQ ID NO: 1, and wherein the Tn3 scaffold is to be administered at an initial dose of 3000 mg of the Tn3 scaffold followed by a second dose of 3000 mg four weeks later and a third dose of 3000 mg about 8 weeks after the second dose, and to be administered at a maintenance dose of about 3000 mg every 12 weeks thereafter.

**[0012c]** In another aspect, the present disclosure refers to a use of Tn3 scaffold comprising SEQ ID NO: 1 in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 scaffold is to be administered at an initial dose of 3000 mg of the Tn3 scaffold followed by a second dose of 3000 mg four weeks later and a third dose of 3000 mg about 8 weeks after the second dose, and to be administered at a maintenance dose of about 3000 mg every 12 weeks thereafter.

**[0012d]** In another aspect, the present disclosure refers to a use of a Tn3 scaffold comprising SEQ ID NO: 1 in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 scaffold is to be administered an initial dose of 3000 mg of the Tn3 scaffold followed by a second dose of 3000 mg four weeks later and a third dose of 3000 mg about 8 weeks after the second dose, and to be administered at a maintenance dose of about 3000 mg every 12 weeks thereafter.

**[0012e]** In another aspect, the present disclosure refers to a use of a Tn3 scaffold comprising SEQ ID NO: 1 in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 scaffold is to be administered at a loading dose of 1500 mg about every 2 weeks for at least 3 doses, and wherein the Tn3 scaffold is to be administered at a maintenance dose of 1500 mg every 4 weeks.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0013] FIG. 1** shows an exemplary study flow diagram comprising adults with moderate to severe (moderate to high) systemic disease activity defined by ESSDAI ≥ 5, and presence of anti-Ro autoantibodies and/or rheumatoid factor (RF). Seventy four subjects were randomized (1:1) to receive VIB4920 1500 mg or placebo intravenously once every 2 weeks x 3 doses, then once every 4 weeks (Q4W) for 4 additional doses (Stage I). Starting on day 169, subjects randomized to VIB4920 received placebo Q4W for 5 doses and subjects randomized to placebo received VIB4920 Q4W for 5 doses (Stage II). Randomization was stratified by EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) score at screening (< 10 points vs ≥ 10 points). Δ = delta; D = days; EoS = End of Study; EP = endpoint; ESSDAI = European League

## CLAIMS

1. Use of a Tn3 scaffold in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the

Tn3 scaffold comprises two CD40L-specific monomer subunits; wherein the Tn3 scaffold comprises SEQ ID NO: 1,

and wherein the Tn3 scaffold is to be administered at a loading dose of 1500 mg about every 2 weeks for at least 3 doses, and wherein the Tn3 scaffold is to be administered at a maintenance dose of 1500 mg every 4 weeks.

2. The use of claim 1, wherein the subject has a European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index (ESSDAI) score ≥ 5.

3. The use of claim 1, wherein the subject has:

(a) a ESSDAI score < 5, and

(b) a EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) score ≥ 5.

4. The use of claim 3, wherein the subject has:

whole stimulated salivary flow > 0.1 mL/min.

5. Use of a Tn3 scaffold comprising SEQ ID NO: 1 in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 scaffold is to be administered at a loading dose of 1500 mg about every 2 weeks for at least 3 doses, and wherein the Tn3 scaffold is to be administered at a maintenance dose of 1500 mg every 4 weeks.

6. Use of a Tn3 scaffold comprising SEQ ID NO: 1 in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 scaffold is to be administered at a loading dose of 1500 mg about every 2 weeks for at least 3 doses, and wherein the Tn3 scaffold is to be administered at a maintenance dose of 1500 mg every 4 weeks.

7. Use of a Tn3 scaffold in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 comprises two CD40L-specific monomer subunits and a human serum albumin;

wherein the Tn3 scaffold comprises SEQ ID NO: 1,

and wherein the Tn3 scaffold is to be administered at an initial dose of 3000 mg of the Tn3 scaffold followed by a second dose of 3000 mg four weeks later and a third dose of 3000 mg about 8 weeks after the second dose, and to be administered at a maintenance dose of about 3000 mg every 12 weeks thereafter.

8. The use of claim 7, wherein the subject has a European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index (ESSDAI) score ≥ 5.

9. The use of claim 7, wherein the subject has:

(a) a ESSDAI score < 5, and

(b) a EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) score ≥ 5.

10. The use of claim 9, wherein the subject has:

whole stimulated salivary flow > 0.1 mL/min.

11. Use of Tn3 scaffold comprising SEQ ID NO: 1 in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 scaffold is to be administered at an initial dose of 3000 mg of the Tn3 scaffold followed by a second dose of 3000 mg four weeks later and a third dose of 3000 mg about 8 weeks after the second dose, and to be administered at a maintenance dose of about 3000 mg every 12 weeks thereafter.

12. Use of a Tn3 scaffold comprising SEQ ID NO: 1 in the manufacture of a medicament for treating Sjögren's syndrome (SS) in a subject in need thereof, wherein the Tn3 scaffold is to be administered at an initial dose of 3000 mg of the Tn3 scaffold followed by a second dose of 3000 mg four weeks later and a third dose of 3000 mg about 8 weeks after the second dose, and to be administered at a maintenance dose of about 3000 mg every 12 weeks thereafter.