CLAIMS

1. Use of teplizumab in the manufacture of a medicament for treating clinical type 1 diabetes (T1D) triggered by a viral infection in a patient in need thereof, wherein the treatment comprises the patient is to be administered two 12-day courses of teplizumab, each 12-day course comprising

a first dose of 106 μg/m^2 teplizumab on day 1,

a second dose of 425 μg/m^2 teplizumab on day 2, and

one dose of 850 μg/m^2 teplizumab on each of days 3–12,

wherein the total teplizumab dose of each course is approximately 9031 μg/m^2.

2. The use of claim 1, wherein the two courses of teplizumab are to be administered at an interval of 6 months to 12 months.

3. The use of claim 1 or 2, wherein the treatment comprises the patient to be administered one or more additional 12-day courses of teplizumab, optionally wherein each additional 12-day course comprises

a first dose of 106 μg/m^2 teplizumab on day 1,

a second dose of 425 μg/m^2 teplizumab on day 2, and

one dose of 850 μg/m^2 teplizumab on each of days 3–12, and

wherein the total teplizumab dose of each additional course is approximately 9031 μg/m^2.

4. The use of claim 3, wherein each additional 12-day course of teplizumab is to be administered at 6 months to 24 months after the preceding course.

5. The use of any one of claims 1-4, wherein

after the administration of each 12-day course, a baseline level of $TIGIT^+KLRG1^+CD8^+$ T cells with respect to all $CD3^+$ T cells is to be determined,

the level of $TIGIT^+KLRG1^+CD8^+CD3^+$ T cells is to be monitored, and

an additional 12-day course of teplizumab is to be administered when the level of $TIGIT^+KLRG1^+CD8^+CD3^+$ T cells returns to the baseline level, optionally

wherein the level of $TIGIT^+KLRG1^+CD8^+CD3^+$ T cells is to be determined and monitored by flow cytometry, further optionally

wherein the level of $TIGIT^+KLRG1^+CD8^+CD3^+$ T cells is to be determined 1-6 months, 2-5 months, or 3 months after the administration of each 12-day course.

6. The use of claim 5, wherein

a) if the patient has more than 10% $TIGIT^+KLRG1^+CD8^+$ T cells in all $CD3^+$ T cells, subsequent monitoring is annual; or

b) if the patient has less than 10% $TIGIT^+KLRG1^+CD8^+$ T cells in all $CD3^+$ T cells,

subsequent monitoring is every 3-6 months.

7. The use of any one of claims 1-6, wherein

a) the patient is post severe acute respiratory syndrome (SARS)-associated coronavirus (SARS-CoV-2) infection; and/or

b) the patient is negative for SARS-CoV-2 infection and positive for type 1 diabetes-associated autoantibodies.

8. The use of any one of claims 1-7, wherein before teplizumab is to be administered to the patient, the patient has been diagnosed with T1D within 6-12 weeks .

9. The use of claim 8, wherein the patient has been diagnosed with T1D within 6 weeks.

10. The use of claim 8, wherein the patient has been diagnosed with T1D within 12 weeks.

11. The use of any one of claims 8-10, wherein teplizumab is to be administered to the subject to result in reduction of insulin use, HbA1c levels, hypoglycemic episodes, or combinations thereof by at least 10% as compared to pre-treatment levels.

12. The use of any one of claims 1-11, wherein the patient has a non-fasting C-peptide level of ≥ 0.2 pmol/mL up to 12 months after T1D diagnosis.

13. The use of any one of claims 1-12, wherein each dose is to be administered parenterally, optionally

by intravenous infusion, further optionally, wherein each dose is to be administered by intravenous infusion over a period of at least 30 minutes.

14. The use of any one of claims 1-13, wherein

a) the patient is 8 to 17 years old;

b) the patient has a peak C-peptide level of ≥0.2 pmol/mL during a mixed meal tolerance test (MMTT);

c) the subject receiving teplizumab has a higher mean C-peptide value compared with a control subject receiving placebo;

d) the patient has at least 20% of beta-cell function prior to the administration of the first dose; and/or

e) the patient is positive for at least one T1D-associated autoantibody selected from the group consisting of glutamic acid decarboxylase 65 (GAD65) autoantibodies, islet antigen 2 (IA-2) autoantibodies, zinc transporter 8 (ZnT8) autoantibodies, and islet cell cytoplasmic autoantibodies (ICA), and optionally insulin autoantibodies (IAA);

f) the patient has symptoms of hyperglycemia; and/or

g) the patient has or has tested positive for at least one of the following:

i) a fasting plasma glucose level of ≥126 mg/dL (7.0 mmol/L);

(ii) a 2-hour plasma glucose level of ≥200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT);

(iii) a hemoglobin A1C (HbA1c) level of ≥6.5% (48 mmol/mol); and

(iv) a random plasma glucose level of ≥200 mg/dL (11.1 mmol/L).

15. The use of any one of claims 1-14, wherein the area under the time-concentration curve (AUC) of C-peptide is to be assessed following a mixed meal tolerance test (MMTT) at 78 weeks.

16. The use of any one of claims 1-15, wherein the reduction of insulin use, HbA1c levels, hypoglycemic episodes, or combinations thereof is over a period of 12 months or more.

17. The use of any one of claims 1-16, wherein the patient receives premedication of a non-steroidal anti-inflammatory drug (NSAID), optionally ibuprofen, acetaminophen, and/or an antihistamine, optionally diphenhydramine,

for at least the first 5 days of the treatment course.