Claims

1. A delta-like ligand 4 (DII4) antagonist for use in preventing, treating or ameliorating diabetes mellitus type 1 in a subject, wherein the antagonist blocks an interaction between DII4 and Notch receptor and diabetes is prevented, treated or ameliorated, and wherein the DII4 antagonist is an antibody or fragment thereof that specifically binds hDII4 and blocks DII4-Notch signal pathways, or a fusion protein comprising the extracellular domain of DII4 that is fused to the Fc domain of a human IgG.

2. A delta-like ligand 4 (DII4) antagonist for use in lowering a blood glucose level associated with diabetes mellitus type 1 in a subject in need thereof, wherein the antagonist blocks an interaction between DII4 and Notch receptor and the blood glucose level is lowered, and wherein the DII4 antagonist is an antibody or fragment thereof that specifically binds hDII4 and blocks DII4-Notch signal pathways, or a fusion protein comprising the extracellular domain of DII4 that is fused to the Fc domain of a human IgG.

3. The DII4 antagonist for use according to any one of the preceding claims, wherein the antibody or fragment thereof comprises a heavy chain variable region (HCVR) comprising heavy chain CDR1, CDR2 and CDR3 sequences of SEQ ID NO:22, 24 and 26, respectively, and a light chain variable region (LCVR) comprising light chain CDR1, CDR2 and CDR3 sequences of SEQ ID NO:30, 32 and 34, respectively.

4. The DII4 antagonist for use according to claim 3, wherein the antibody or fragment thereof comprises (a) a HCVR sequence of SEQ ID NO:20 or 116 and a LCVR sequence of SEQ ID NO:28 or 118, or (b) a HCVR/LCVR combination of SEQ ID NO:20/28 or 116/118.

5. The DII4 antagonist for use according to any one of the preceding claims in combination with at least one additional therapeutic agent selected from blood glucose lowering agent, immunosuppressant, anti-inflammatory agent, and analgesic agent, optionally wherein:

   (i) the additional therapeutic agent is at least one selected from the group consisting of insulin or analogues thereof, glucocorticoids, cyclosporin, methotrexate, non-steroidal anti-inflammatory drugs (NSAIDs), TNF-α antagonists, IL-1 antagonists, IL-6 antagonists, and opioids; and/or
   (ii) the DII4 antagonist and at least one additional therapeutic agent are for concurrent or sequential administration.

6. Use of a delta-like ligand 4 (DII4) antagonist in the manufacture of a medicament for preventing, treating or ameliorating diabetes mellitus type 1 in a subject, wherein the antagonist blocks an interaction between DII4 and Notch receptor, and

wherein the DII4 antagonist is an antibody or fragment thereof that specifically binds hDII4 and blocks DII4- Notch signal pathways, or a fusion protein comprising the extracellular domain of DII4 that is fused to the Fc domain of a human IgG.

7. Use of a delta-like ligand 4 (DII4) antagonist in the manufacture of a medicament for lowering a blood glucose level associated with diabetes mellitus type 1 in a subject, wherein the antagonist blocks an interaction between DII4 and Notch receptor, and
wherein the DII4 antagonist is an antibody or fragment thereof that specifically binds hDII4 and blocks DII4-Notch signal pathways, or a fusion protein comprising the extracellular domain of DII4 that is fused to the Fc domain of a human IgG.

8. The use according to claim 6 or 7, wherein the antibody or fragment thereof comprises a heavy chain variable region (HCVR) comprising heavy chain CDR1, CDR2 and CDR3 sequences of SEQ ID NO:22, 24 and 26, respectively, and a light chain variable region (LCVR) comprising light chain CDR1, CDR2 and CDR3 sequences of SEQ ID NO:30, 32 and 34, respectively.

9. The use according to claim 8, wherein the antibody or fragment thereof comprises (a) a HCVR sequence of SEQ ID NO:20 or 116, and a LCVR sequence of SEQ ID NO:28 or 118, or (b) a HCVR/LCVR combination of SEQ ID NO:20/28 or 116/118.