heterocyclic ring system containing one to two heteroatoms selected from O, S, and N, the fused ring system being unsubstituted or substituted with one to two substituents selected from hydroxy, amino, fluorine, $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy, and trifluoromethyl.

**[0015]** In some embodiments, the engineered transaminase polypeptide are capable of biocatalytic conversion of compounds of Formula **(II)** to compounds of Formula **(I)** having the indicated stereochemical configuration at the stereogenic center marked with an *; in an enantiomeric excess of *at least 70% over the opposite enantiomer.*

**[0016]** In one aspect, there is provided an engineered polypeptide having transaminase activity comprising an amino acid sequence having at least 80% sequence identity to reference sequence of SEQ ID NO:2, an amino acid residue difference as compared to SEQ ID NO:2 at position 126, wherein said amino acid residue at position 126 is alanine, and (a) an amino acid residue difference as compared to SEQ ID NO:2 selected from X33L, X36C, X41C/F/K/M/N/R, X42G, X48D/E/G/K/T, X51K, X54P, X76S, X122F/Q, X148Q, X152T, X155A/I/K/T/V, X156R, X160P, X215G/H/L, X241R, X270T, X273H, X325M; and X241R, or (b) a combination of residue differences selected from: X42G, X54P, X152S, and X155T; X42G, X54P, X152S, X155T, and R164P; X42G, X54P, X150F, X152S, and X155T; X42G, X54P, X150F, X152S, X155T, and X267V; X42G, X54P, X150F, X152S, X155L, W156Q, and C215G; X42G, X54P, X150F, X152S, X155T, X215G, and X267V; X33L; X42G, X54P, X117G; X150F, X152S, X155I, X156Q, and C215G; and X41K, X42G, X54P, X150F, X152S, X155K, X156Q, and C215G; X33L, X42G, X54P, X109S, X150F, X152S, X155K, X156Q, and X215H; X33L, X42G, X54P, X150F, X152S, X155I, X156Q, and X215G; X33L, X42G, X54P, X150F, X152S, X155K, X156Q, and X215H; X33L, X42G, X54P, X150F, X152S, X155L, X156Q, and X215H; X33L, X42G, X54P, X150F, X152S, X155L, X156Q, X215H, and X241R; X41F, X42G, X54P, X122Q, X150F, X152T, X155V, X156Q, and X215G; X41F, X42G, X54P, X150F, X152S, X155L, X156Q, X171I, *X215G, and X241R; X41F, X42G, X54P, X150F, X152S, X155I, X156Q,* V171I, *and X215G;* X41F, X42G, X54P, X150F, X152S, X155I, X156Q, and X215G; X41F, X42G, X54P, X150F, X152S, X155L, X156Q, X171I, and X215G; X41F, X42G, X54P, X150F, X152S, X155L, X156Q, and X215G; X42G, X48G, X54P, X150F, X152S, X155L, X156Q, and X215H; X42G, X54P, X60V, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X68A, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X69S, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X122Q, X150F, X152S, X155I, X156Q, X215G, and X241R; X42G, X54P, X122Q, X150F, X152S, X155L, X156Q, X171I, X215G, and X241R; X42G, X54P, X122Q, X150F, X152T, X155V, X156Q, X171I, X215G, and X241R~~; X42G, X54P, X126M, X150F, X152S, X155L, X156Q, and X215G~~; X42G, X54P, X135I, X136Y, X150F, X152S, X155L,

X156Q, X215G, X282V, and X284P; X42G, X54P, X150F, X152S, X155I, X156Q, X171I, X215G, and X241R; X42G, X54P, X150F, X152S, X155L, X156Q, X193M, and X215G; X42G, X54P, X150F, X152S, X155L, X156Q, X215G, X282V, and X284I; X42G, X54P, X150F, X152S, X155L, X156Q, X215G, and X283S; X42G, X54P, X150F, X152S, X155L, X156Q, X215G, and X284I; and X42G, X54P, X150F, X152S, X155L, X156Y, and X215G.

**[0017]** In some embodiments of the engineered polypeptides having transaminase activity of the present disclosure, the amino acid sequence can further comprise one or more residue differences as compared to SEQ ID NO:2 selected from: X5K, X33L, X36C, X41C/F/K/M/N/R, X42A/G, X44Q, X48D/E/G/K/T, X49T, X51K, X54P, X55L, X76S, X108V, X117G, X122F/Q, X126A, X148Q, X150A/F, X152S/T, X155A/I/K/L/T/V, X156Q/R/S, X160P, X164P, X165N, X182T, X215G/H/L, X218M, X241R, X267V, X270T, X273H, X325M, and X328I.

**[0018]** ~~In one aspect, there is provided~~Disclosed is an engineered polypeptide having transaminase activity comprising an amino acid sequence having at least 80% sequence identity to reference sequence of SEQ ID NO:2 and (a) an amino acid residue difference as compared to SEQ ID NO:2 selected from G36C, I41C, I41F, I41K, I41M, I41N, I41R, E42G, P48D, P48E, P48G, P48K, P48T, A51K, S54P, M122F, M122Q, Y148Q, C152T, Q155A, Q155I, Q155K, Q155T, Q155V, C215H, C215L, Y273H, L325M, and A241R; or (b) a combination of residue differences selected from: A5K, E42G, S49T, S54P, C152S, Q155T, and W156Q; P33L, I41C, E42G, S54P, S150F, C152S, Q155K, F160P, and C215G; P33L, I41K, E42G, S54P, S150F, C152S, Q155I, F160P, and C215L; P33L, E42G, P48G, S54P, S150F, C152S, Q155T, and C215H; P33L, E42G, S54P, A109S, S150F, C152S, Q155K, W156Q, and C215H; P33L, E42G, S54P, E117G, S150F, C152S, Q155I, W156Q, and C215G; P33L, E42G, S54P, S150F, C152S, Q155I, W156Q, and C215G; P33L, E42G, S54P, S150F, C152S, Q155K, W156Q, and C215H; P33L, E42G, S54P, S150F, C152S, Q155L, W156Q, and C215H; P33L, E42G, S54P, S150F, C152S, Q155L, W156Q, C215H, and A241R; G36C, E42G, P48G, S54P, S150F, C152S, Q155I. and C215H; G36C, E42G, P48K, S54P, S150F, C152S, Q155T, and C215H; G36C, E42G, S54P, S150F, C152S, Q155I, C215H, and A241R; G36C, E42G, S54P, S150F, C152S, Q155K, C215H, and A241R; G36C, E42G, S54P, S150F, C152S, Q155T, and A241R; G36C, E42G, S54P, S150F, C152S, Q155V, and C215H; I41C, E42G, S49T, S54P, S150F, C152S, Q155I, F160P, C215G, and I267V; I41C, E42G, S49T, S54P, S150F, C152S, Q155K, W156Q, C215G and I267V; I41C, E42G, S54P, I108V, S150F, C152S, and Q155K; I41C, E42G, S54P, I108V, S150F, C152S, Q155K, W156Q, C215G, and I267V; I41C, E42G, S54P, I108V, S150F, C152S, Q155T, W156Q, and C215G; I41C, E42G, S54P, E117G, S150F, C152S, Q155K, and F160P; I41C, E42G, S54P, E117G, S150F, C152S, Q155K, and C215L; I41C, E42G, S54P, E117G, S150F, C152S, Q155L, and C215L; I41C, E42G, S54P, S150F, C152S, Q155I, and C215G; I41C, E42G, S54P, S150F, C152S, Q155I, and C215L; I41C, E42G, S54P, S150F, C152S, Q155K, W156Q, C215G, and I267V; I41C, E42G, S54P, S150F, C152S, Q155K, and

**What is claimed is:**

1. An engineered polypeptide having transaminase activity comprising an amino acid sequence having at least 80% sequence identity to reference sequence of SEQ ID NO:2, an amino acid residue difference as compared to SEQ ID NO:2 at position 126, wherein said amino acid residue at position 126 is alanine, and

(a) an amino acid residue difference as compared to SEQ ID NO:2 selected from X33L, X36C, X41C/F/K/M/N/R, X42, X48D/E/G/K/T, X51K, X54, X76S, X122F/Q, X148Q, X152T, X155A/I/K/T/V, X156R, X160P, X215G/H/L, X241R, X270T, X273H, X325M and X241R; or

(b) a combination of residue differences selected from: X42G, X54P, X152S, and X155T; X42G, X54P, X152S, X155T, and R164P; X42G, X54P, X150F, X152S, and X155T; X42G, X54P, X150F, X152S, X155T, and X267V; X42G, X54P, X150F, X152S, X155L, W156Q, and C215G; X42G, X54P, X150F, X152S, X155T, X215G, and X267V; X33L; X42G, X54P, X117G; X150F, X152S, X155I, X156Q, and C215G; X41K, X42G, X54P, X150F, X152S, X155K, X156Q, and C215G; X33L, X42G, X54P, X109S, X150F, X152S, X155K, X156Q, and X215H; X33L, X42G, X54P, X150F, X152S, X155I, X156Q, and X215G; X33L, X42G, X54P, X150F, X152S, X155K, X156Q, and X215H; X33L, X42G, X54P, X150F, X152S, X155L, X156Q, and X215H; X33L, X42G, X54P, X150F, X152S, X155L, X156Q, X215H, and X241R; X41F, X42G, X54P, X122Q, X150F, X152T, X155V, X156Q, and X215G; X41F, X42G, X54P, X150F, X152S, X155L, X156Q, X171I, X215G, and X241R; X41F, X42G, X54P, X150F, X152S, X155I, X156Q, V171I, and X215G; X41F, X42G, X54P, X150F, X152S, X155I, X156Q, and X215G; X41F, X42G, X54P, X150F, X152S, X155L, X156Q, X171I, and X215G; X41F, X42G, X54P, X150F, X152S, X155L, X156Q, and X215G; X42G, X48G, X54P, X150F, X152S, X155L, X156Q, and X215H; X42G, X54P, X60V, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X68A, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X69S, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X122Q, X150F, X152S, X155I, X156Q, X215G, and X241R; X42G, X54P, X122Q, X150F, X152S, X155L, X156Q, X171I, X215G, and X241R; X42G, X54P, X122Q, X150F, X152T, X155V, X156Q, X171I, X215G, and X241R; X42G, X54P, X135I, X136Y, X150F, X152S, X155L, X156Q, X192F, and X215G; X42G, X54P, X136I, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X136I, X150F, X152S, X155L, X156Q, X215G, and X224I; X42G, X54P, X136I, X150F, X152S, X155L, X156Y, X215G, X282V, and X284I; X42G, X54P, X136I, X150F, X152S, X155L, X156Y, X215G, and X284P; X42G, X54P, X136Y, X150F, X152S, X155L, X156Q, X215G, X282V, and X284P; X42G, X54P, X150F, X152S, X155I, X156Q, X171I, X215G, and X241R; X42G, X54P, X150F, X152S, X155L, X156Q, X193M, and X215G; X42G, X54P, X150F, X152S, X155L, X156Q, X215G, X282V, and X284I; X42G, X54P, X150F, X152S, X155L, X156Q, X215G, and X283S; X42G, X54P, X150F, X152S, X155L, X156Q, X215G, and X284I; X42G, X54P, X150F, X152S, X155L, X156Y, and X215G.

2. The engineered polypeptide of Claim 1, in which the amino acid sequence further comprises one or more residue differences as compared to SEQ ID NO:2, selected from: X5K, X33L, X36C, X41C/F/K/M/N/R, X42A/G, X44Q, X48D/E/G/K/T, X49T, X51K, X54P, X55L, X76S, X108V, X117G, X122F/Q, X148Q, X150A/F, X152S/T, X155A/I/K/L/T/V, X156Q/R/S, X160P, X164P, X165N, X182T, X215G/H/L, X218M, X241R, X267V, X270T, X273H, X325M, and X328I.

3. The engineered polypeptide of claim 1 or 2 further comprising:

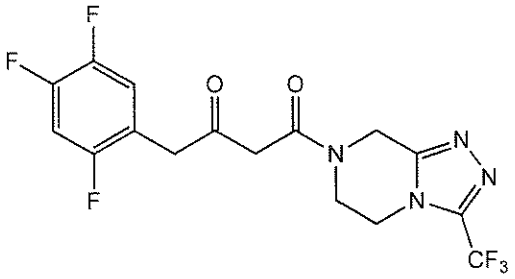
(a) an amino acid residue difference as compared to SEQ ID NO:2 selected from G36C, I41C, I41F, I41K, I41M, I41N, I41R, E42G, P48D, P48E, P48G, P48K, P48T, A51K, S54P, M122F, M122Q, Y148Q, C152T, Q155A, Q155I, Q155K, Q155T, Q155V, C215H, C215L, Y273H, L325M, and A241R; or

(b) a combination of residue differences selected from: A5K, E42G, S49T, S54P, C152S, Q155T, and W156Q; P33L, I41C, E42G, S54P, S150F, C152S, Q155K, F160P, and C215G; P33L, I41K, E42G, S54P, S150F, C152S, Q155I, F160P, and C215L; P33L, E42G, P48G, S54P, S150F, C152S, Q155T, and C215H; P33L, E42G, S54P, A109S, S150F, C152S, Q155K, W156Q, and C215H; P33L, E42G, S54P, E117G, S150F, C152S, Q155I, W156Q, and C215G; P33L, E42G, S54P, S150F, C152S, Q155I, W156Q, and C215G; P33L, E42G, S54P, S150F, C152S, Q155K, W156Q, and C215H; P33L, E42G, S54P, S150F, C152S, Q155L, W156Q, and C215H; P33L, E42G, S54P, S150F, C152S, Q155L, W156Q, C215H, and A241R; G36C, E42G, P48G, S54P, S150F, C152S, Q155I, and C215H; G36C, E42G, P48K, S54P, S150F, C152S, Q155T, and C215H; G36C, E42G, S54P, S150F, C152S, Q155I, C215H, and A241R; G36C, E42G, S54P, S150F, C152S, Q155K, C215H, and A241R; G36C, E42G, S54P, S150F, C152S, Q155T, and A241R; G36C, E42G, S54P, S150F, C152S, Q155V, and C215H; I41C, E42G, S49T, S54P, S150F, C152S, Q155I, F160P, C215G, and I267V; I41C, E42G, S49T, S54P, S150F, C152S, Q155K, W156Q, C215G and I267V; I41C, E42G, S54P, I108V, S150F, C152S, and Q155K; I41C, E42G, S54P, I108V, S150F, C152S, Q155K, W156Q, C215G, and I267V; I41C, E42G, S54P, I108V, S150F, C152S, Q155T, W156Q, and C215G; I41C, E42G, S54P, E117G, S150F, C152S, Q155K, and F160P; I41C, E42G, S54P, E117G, S150F, C152S, Q155K, and C215L; I41C, E42G, S54P, E117G, S150F, C152S, Q155L, and C215L; I41C, E42G, S54P, S150F, C152S, Q155I, and C215G; I41C, E42G, S54P, S150F, C152S, Q155I, and C215L; I41C, E42G, S54P, S150F, C152S, Q155K, W156Q, C215G, and I267V; I41C, E42G, S54P, S150F, C152S, Q155K, and C215L; I41C, E42G, S54P, S150F, C152S, Q155K, and C215G; I41C, E42G, S54P, S150F, C152S, Q155L, F160P, C215G, and I267V; I41C, E42G, S54P, S150F, C152S, Q155T, W156Q, F160P, and C215L; I41C, E42G, S54P, S150F, C152S, Q155T, W156Q, and C215L; I41F, E42G, S54P, M122Q, S150F, C152T, Q155V, W156Q, and C215G; I41F, E42G, S54P, S150F, C152S, Q155L, W156Q, V171I, and C215G; I41F, E42G, S54P, S150F, C152S, Q155L,W156Q,V171I, C215G, and A241R; I41F, E42G, S54P, S150F, C152S, Q155I, W156Q, and C215G; I41K, E42G, P48E, S54P, S150F, C152S, Q155K, and W156Q; I41K, E42G, P48E, S54P, S150F, C152S, Q155L, and C215L; I41K, E42G, S54P, I108V,

E117G, S150F, C152S, Q155K, and C215L; I41K, E42G, S54P, I108V, S150F, C152S, Q155T, and C215G; I41K, E42G, S54P, E117G, S150F, C152S, Q155L, and C215G; I41K, E42G, S54P, E117G, S150F, C152S, Q155K, C215L, and I267V; I41K, E42G, S54P, S150F, C152S, Q155K, W156Q, and C215G; I41K, E42G, S54P, S150F, C152S, Q155K, F160P, C215G, and I267V; I41K, E42G, S54P, S150F, C152S, Q155K, andC215L; I41K, E42G, S54P, S150F, C152S, and Q155T; I41K, E42G, S54P, S150F, C152S, Q155T, and F160P; I41K, E42G, S54P, S150F, C152S, Q155T, and C215G; I41K, E42G, S54P, S150F, C152S, Q155T, C215G, and I267V; I41K, E42G, S54P, S150F, C152S, Q155K, W156Q, and C215G; I41N, E42G, S54P, S150F, C152S, Q155I, and F160P; I41N, E42G, S54P, E117G, S150F, C152S, Q155T; and W156Q; I41N, S49T, E42G, S54P, S150F, C152S, Q155L, F160P, D165N, and C215L; E42A, A44Q, S54P, I108V, S150F, C152S, Q155T, and I267V; E42G, A44Q, S54P, I108V, S150F, C152S, and Q155T; E42G, A44Q, S54P, I108V, S150F, C152S, Q155T, and I267V; E42G, A44Q, S54P, S150A, C152S, and Q155T; E42G, A44Q, S54P, S150F, C152S, and Q155T; E42G, P48G, S54P, S150F, C152S, Q155L, W156Q, and C215H; E42G, P48G, S54P, S150F, C152S, and Q155T; E42G, S49T, S54P, I108V, E117G, S150F, C152S, Q155L, F160P, and C215L; E42G, S49T, S54P, I108V, E117G, S150F, C152S, Q155K, W156Q, and C215G; E42G, S49T, S54P, I108V, E117G, S150F, C152S, Q155T, W156Q, C215G, and I267V; E42G, S49T, S54P, C152S, Q155T, and W156Q; E42G, S54P, I55L, T126A, C152S, Q155T, L218M, and A270T; E42G, S54P, F60V, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, T68A, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, T69S, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, N76S, T126A, C152S, Q155T, S182T, L218M, A270T, and V328I; E42G, S54P, I108V, S150F, C152S, Q155K, and C215H; E42G, S54P, I108V, S150F, C152S, and Q155T; E42G, S54P, I108V, S150F, C152S, Q155T, and I267V; E42G, S54P, I108V, S150F, C152S, Q155V, W156Q, and F160P; E42G, S54P, E117G, C152S, and Q155T; E42G, S54P, E117G, C152S, Q155T, and W156Q; E42G, S54P, M122Q, S150F, C152S, Q155I, W156Q, C215G, and A241R; E42G, S54P, M122Q, S150F, C152S, Q155L,W156Q, V171I, C215G, and A241R; E42G, S54P, M122Q, S150F, C152T, Q155V, W156Q, V171I, C215G, and A241R; E42G, S54P, P135I, F136Y, S150F, C152S, Q155L, W156Q, W192F, and C215G; E42G, S54P, F136I, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, F136I, S150F, C152S, Q155L, W156Q, C215G, and G224I; E42G, S54P, F136I, S150F, C152S, Q155L, W156Y, C215G, S282V, and G284I; E42G, S54P, F136I, S150F, C152S, Q155L, W156Y, C215G, and G284P; E42G, S54P, F136Y, S150F, C152S, Q155L, W156Q, C215G, S282V, and G284P; E42G, S54P, S150A, C152S, Q155T, and I267V; E42G, S54P, S150F, C152S, Q155I, W156Q, F160P, C215L, and I267V; E42G, S54P, S150F, C152S, Q155I, W156Q, V171I, C215G, and A241R; E42G, S54P, S150F, C152S, Q155I, W156Q, and C215L; E42G, S54P, S150F, C152S, Q155I, F160P, and C215G; E42G, S54P, S150F, C152S, Q155I, and C215H; E42G, S54P, S150F, C152S, Q155K, and W156Q; E42G, S54P, S150F, C152S, Q155K, W156Q, and I267V; E42G, S54P, S150F, C152S, Q155L, W156Q, G193M, and C215G; E42G, S54P, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, S150F, C152S, Q155L, W156Q, C215G, S282V, and G284I; E42G, S54P, S150F, C152S, Q155L, W156Q, C215G, and T283S; E42G, S54P, S150F, C152S, Q155L,

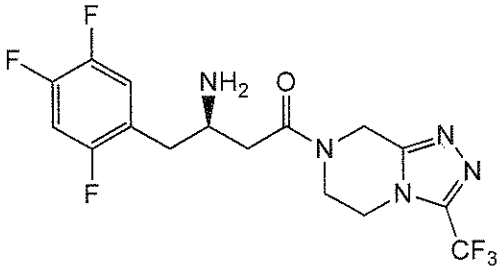
W156Q, C215G, and G284I; E42G, S54P, S150F, C152S, Q155L, W156Y, and C215G; E42G, S54P, S150F, C152S, Q155L, and C215H; E42G, S54P, S150F, C152S, and Q155T; E42G, S54P, S150F, C152S, Q155T, C215G, and I267V; E42G, S54P, S150F, C152S, Q155T, and I267V; E42G, S54P, S150F, C152S, Q155T, W156Q, F160P, C215L, and I267V; E42G, S54P, S150F, C152S, Q155T, W156Q, C215G, and I267V; E42G, S54P, S150F, C152S, Q155T, and W156R; E42G, S54P, S150F, C152S, Q155T, F160P, and C215G; E42G, S54P, S150F, C152S, Q155T, F160P, and C215L; E42G, S54P, S150F, C152S, Q155T, C215G, and I267V; E42G, S54P, S150F, C152S, Q155T, and I267V; E42G, S54P, C152S, Q155I, and W156S; E42G, S54P, C152S, Q155K, and W156S; E42G, S54P, C152S, Q155L, and W156S; E42G, S54P, C152S, and Q155T; E42G, S54P, C152S, Q155T, and F160P; E42G, S54P, C152S, Q155T, and R164P; E42G, S54P, C152S, Q155T, and W156Q; E42G, S54P, C152S, Q155T, and W156S; E42G, S54P, C152S, Q155T, and R164P; E42G, S54P,C152S, Q155T, S182T, L218M, and A270T; E42G, S54P, C152S, Q155T, and C215G; E42G, S54P, C152S, Q155T, and C215L; and E42G, S54P, C152S, Q155V, and W156S.

4. The engineered polypeptide of Claim 1, wherein said engineered polypeptide is capable of converting a substrate compound (**2**)



**(2)**

to a product compound (**1**)



**(1)**

under suitable reaction conditions.

5. The engineered polypeptide of Claim 4, which is capable of converting compound (**2**) to compound (**1**) with at least 1.2 fold the activity of SEQ ID NO:2 under suitable reaction conditions.

6. The engineered polypeptide of Claim 5, in which the suitable reaction conditions comprise compound **(2)** loading of at least 50 g/L, 1 mM PLP, 50% DMSO (v/v), 1.5 M isopropylamine, pH 11, and 55°C.

7. The engineered polypeptide of Claim 1, in which the amino acid sequence comprises a sequence selected from SEQ ID NO: 86 and 88.

8. The engineered polypeptide of Claim 1, in which the polypeptide is immobilized on a solid support.

9. The engineered polypeptide of Claim 8, in which the solid support is a bead or resin comprising polymethacrylate with epoxide functional groups, polymethacrylate with amino epoxide functional groups, styrene/DVB copolymer or polymethacrylate with octadecyl functional groups.

10. A polynucleotide encoding the engineered polypeptide of any one of Claims 1 to 7.

11. The polynucleotide of Claim 10, further comprising a nucleotide sequence selected from SEQ ID NO: 85 and 87.

12. An expression vector comprising the polynucleotide of Claim 10 or 11.

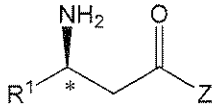
13. The expression vector of Claim 12, comprising at least one control sequence.

14. A host cell comprising the polynucleotide of Claim 10 or 11 or the expression vector of Claim 12 or 13.

15. A method of preparing the engineered polypeptide of any one of Claims 1 to 7, comprising culturing the host cell of Claim 14, under conditions suitable for expression of the polypeptide.

16. The method of Claim 15, further comprising isolating the polypeptide.

17. A process for preparing a compound of structural Formula **(I)**:




**(I)**

having the indicated stereochemical configuration at the stereogenic center marked with an *; in an enantiomeric excess of at least 70% over the opposite enantiomer,

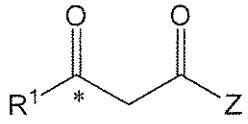
wherein

Z is $OR^2$ or $NR^2R^3$;

$R^1$ is $C_{1-8}$ alkyl, aryl, heteroaryl, aryl-$C_{1-2}$ alkyl, heteroaryl-$C_{1-2}$ alkyl, or or a 5- to 6-membered heterocyclic ring system optionally containing an additional heteroatom selected from O, S, and N, the heterocyclic ring being unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, $C_{1-4}$ alkoxy, and $C_{1-4}$ alkyl, wherein alkyl and alkoxy are unsubstituted or substituted with one to five fluorines;

$R^2$ and $R^3$ are each independently hydrogen, $C_{1-8}$ alkyl, aryl, or aryl-$C_{1-2}$ alkyl; or

$R^2$ and $R^3$ together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclic ring system optionally containing an additional heteroatom selected from O, S, and N, the heterocyclic ring being unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, $C_{1-4}$ alkoxy, and $C_{1-4}$ alkyl, wherein alkyl and alkoxy are unsubstituted or substituted with one to five fluorines; and the heterocyclic ring system being optionally fused with a 5- to 6-membered saturated or aromatic carbocyclic ring system or a 5- to 6-membered saturated or aromatic heterocyclic ring system containing one to two heteroatoms selected from O, S, and N, the fused ring system being unsubstituted or substituted with one to two substituents selected from hydroxy, amino, fluorine, $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy, and trifluoromethyl; the process comprising the step of contacting a compound of structural Formula (**II**):



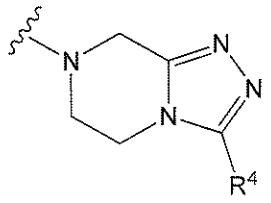

**(II)**

with an engineered polypeptide of any one of Claims 1 to 9 in the presence of an amino group donor in a suitable organic solvent under suitable reaction conditions.

18. The process of Claim 17, wherein $R^1$ is benzyl wherein the phenyl group of benzyl is unsubstituted or substituted one to three substituents selected from the group consisting of fluorine, trifluoromethyl, and trifluoromethoxy.

19. The process of Claim 17, wherein Z is $NR^2R^3$.

20. The process of Claim 19, wherein $NR^2R^3$ is a heterocycle of the structural Formula **(III)**:

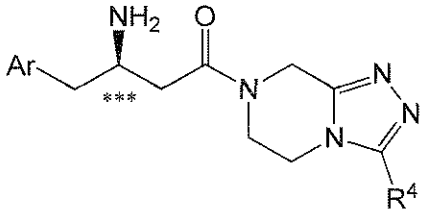


**(III)**

wherein $R^4$ is hydrogen or $C_{1-4}$ alkyl which is unsubstituted or substituted with one to five fluorines.

21. The process of any one of Claims 17 to 20, wherein the compound of structural Formula **(II)** excludes compound **(2)** and the compound of structural Formula **(I)** excludes compound **(1)**.

22. A process for preparing a compound of structural Formula **(Ia)**:



**(Ia)**

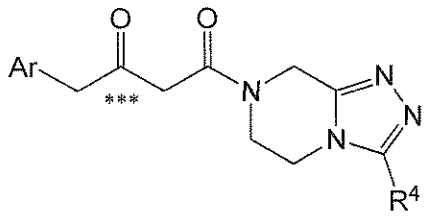
having the (*R*)-configuration at the stereogenic center marked with an ***; in an enantiomeric excess of at least 70% over the enantiomer having the opposite (*S*)-configuration;

wherein,

Ar is phenyl which is unsubstituted or substituted with one to five substituents independently selected from the group consisting of fluorine, trifluoromethyl, and trifluoromethoxy; and

$R^4$ is hydrogen or $C_{1-4}$ alkyl unsubstituted or substituted with one to five fluorines; the process comprising the step of:

contacting a prochiral ketone of structural Formula **(IIa)**:



**(IIa)**

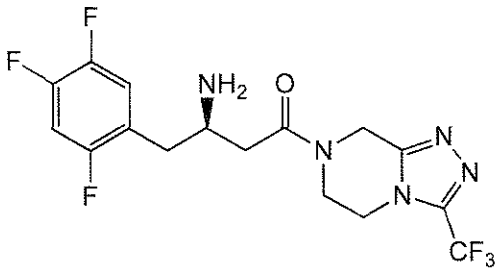
with an engineered polypeptide of any one of Claims 1 to 9, in the presence of an amino group donor under suitable reaction conditions.

23. The process of Claim 22, wherein Ar is 2,5-difluorophenyl or 2,4,5-trifluorophenyl and $R^4$ is trifluoromethyl.

24. The process of Claim 23, wherein Ar is 2,4,5-trifluorophenyl.

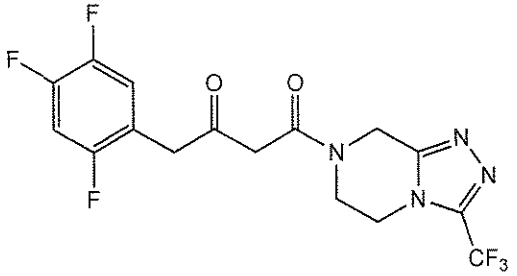
25. The process of any one of Claims 22 to 24, wherein the compound of structural Formula (**IIa**) exclude compound **(2)** and the compound of structural Formula (**Ia**) excludes compound **(1)**.

26. A process of preparing compound **(1)**



**(1)**

comprising a step of contacting a substrate of compound **(2)**



**(2)**

with an engineered polypeptide of any one of Claims 1 to 9, in the presence of an amino group donor under suitable reaction conditions.

27. The process of any one of Claims 17 to 26, wherein the compound of Formula **(I)**, the compound of Formula **(Ia)**, or the compound **(1)** is produced in at least 90% enantiomeric excess.

28. The process of any one of Claims 17 to 26, wherein the compound of Formula **(I)**, the compound of Formula **(Ia)**, or the compound **(1)** is produced in at least 99% enantiomeric excess.

29. The process of any one of Claims 17 to 26, wherein the amino group donor is selected from isopropylamine, alanine, 3-aminobutyric acid, or methylbenzylamine.

30. The process of Claim 29, wherein the amino group donor is isopropylamine, optionally at a concentration of about 0.1 to about 3.0 M, 0.2 to about 2.5 M, about 0.5 to about 2 M or about 1 to about 2 M.

31. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise a pH of from about pH 9.5 to about pH 11.5.

32. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise a temperature of about 45°C to about 60°C.

33. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise dimethylsulfoxide (DMSO) at about 30% (v/v) to about 60% (v/v).

34. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise the substrate compound at a loading of about 5 g/L to about 200 g/L, about 10 g/L to about 150 g/L, or about 50 g/L to about 100 g/L.

35. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise the engineered polypeptide at a concentration of from about 0.5 g/L to about 5 g/L, about 0.5 g/L to about 3 g/L, about 0.5 g/L to about 2 g/L, or from about 0.5 g/L to about 1 g/L.

36. The process of Claim 26, wherein the suitable reaction conditions comprise: (a) substrate loading of about 10 to 200 g/L of substrate compound **(2)**; (b) engineered polypeptide concentration of about 0.5 g/L to 5 g/L; (c) IPM concentration of about 0.1 to 3 M; (d) PLP cofactor concentration of about 0.1 to 1 mM; (e) DMSO concentration of about 30% (v/v) to about 60% (v/v); (f) pH of about 9.5 to 11.5; and (g) temperature of about 45°C to 60°C.

37. The process of Claim 26, wherein the suitable reaction conditions comprise: (a) about 50 g/L of substrate compound **(2)**; (b) about 2 g/L engineered polypeptide; (c) about 50% (v/v) dimethylsulfoxide (DMSO); (d) about 1 M isopropylamine (IPM); (e) about 1 mM pyridoxal phosphate (PLP); (f) about pH 10; and (g) about 50°C.

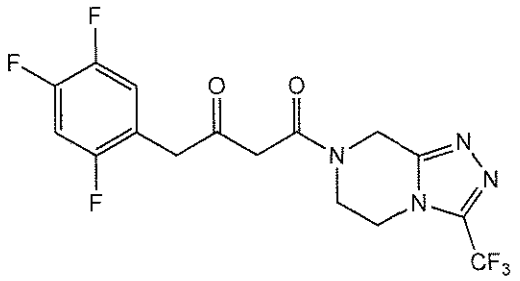
38. The process of any one of Claims 17 to 26, further comprising the step of isolating the compound of Formula **(I)**, the compound of Formula **(Ia)**, or the compound **(1)** from the reaction.

39. The process of any one of Claims 17 to 26, further comprising the step of converting the compound of Formula **(Ia)**, or the compound **(1)** into a pharmaceutically acceptable salt by contacting said compound with a pharmaceutically acceptable acid in a suitable reaction solvent.

40. The process of Claim 39, wherein the pharmaceutically acceptable acid is phosphoric acid and the pharmaceutically acceptable salt is the dihydrogen phosphate salt.

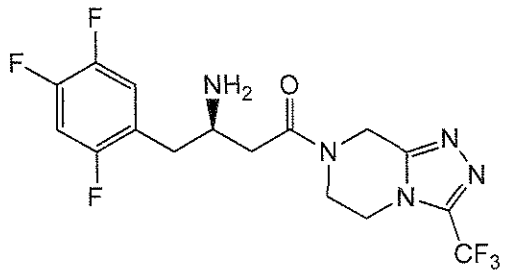
41. The process of Claim 40, further comprising the step of crystallizing the pharmaceutically acceptable salt from the reaction solvent.

42. A process for the preparation of (2*R*)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine phosphate (1:1) monohydrate, the process comprising a step of converting a substrate compound (**2**)



**(2)**

to a product compound (**1**)



**(1)**

by contacting a substrate of compound **(2)** with an engineered polypeptide of any one of Claims 1 to 9, in the presence of an amino group donor under suitable reaction conditions.

43. The method of Claim 42, in which the amino group donor is isopropylamine.

**What is claimed is:**

1. An engineered polypeptide having transaminase activity comprising an amino acid sequence having at least 80% sequence identity to reference sequence of SEQ ID NO:2 and

(a) an amino acid residue difference as compared to SEQ ID NO:2 selected from X33L, X36C, X41C/F/K/M/N/R, X42, X48D/E/G/K/T, X51K, X54, X76S, X122F/Q, X148Q, X152T, X155A/I/K/T/V, X156R, X160P, X215G/H/L, X241R, X270T, X273H, X325M and X241R; or

(b) a combination of residue differences selected from: X42G, X54P, X152S, and X155T; X42G, X54P, X152S, X155T, and R164P; X42G, X54P, X150F, X152S, and X155T; X42G, X54P, X150F, X152S, X155T, and X267V; X42G, X54P, X150F, X152S, X155L, W156Q, and C215G; X42G, X54P, X150F, X152S, X155T, X215G, and X267V; X33L; X42G, X54P, X117G; X150F, X152S, X155I, X156Q, and C215G; X41K, X42G, X54P, X150F, X152S, X155K, X156Q, and C215G; X33L, X42G, X54P, X109S, X150F, X152S, X155K, X156Q, and X215H; X33L, X42G, X54P, X150F, X152S, X155I, X156Q, and X215G; X33L, X42G, X54P, X150F, X152S, X155K, X156Q, and X215H; X33L, X42G, X54P, X150F, X152S, X155L, X156Q, and X215H; X33L, X42G, X54P, X150F, X152S, X155L, X156Q, X215H, and X241R; X41F, X42G, X54P, X122Q, X150F, X152T, X155V, X156Q, and X215G; X41F, X42G, X54P, X150F, X152S, X155L, X156Q, X171I, X215G, and X241R; X41F, X42G, X54P, X150F, X152S, X155I, X156Q, V171I, and X215G; X41F, X42G, X54P, X150F, X152S, X155I, X156Q, and X215G; X41F, X42G, X54P, X150F, X152S, X155L, X156Q, X171I, and X215G; X41F, X42G, X54P, X150F, X152S, X155L, X156Q, and X215G; X42G, X48G, X54P, X150F, X152S, X155L, X156Q, and X215H; X42G, X54P, X60V, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X68A, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X69S, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X122Q, X150F, X152S, X155I, X156Q, X215G, and X241R; X42G, X54P, X122Q, X150F, X152S, X155L, X156Q, X171I, X215G, and X241R; X42G, X54P, X122Q, X150F, X152T, X155V, X156Q, X171I, X215G, and X241R; X42G, X54P, X126M, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X135I, X136Y, X150F, X152S, X155L, X156Q, X192F, and X215G; X42G, X54P, X136I, X150F, X152S, X155L, X156Q, and X215G; X42G, X54P, X136I, X150F, X152S, X155L, X156Q, X215G, and X224I; X42G, X54P, X136I, X150F, X152S, X155L, X156Y, X215G, X282V, and X284I; X42G, X54P, X136I, X150F, X152S, X155L, X156Y, X215G, and X284P; X42G, X54P, X136Y, X150F, X152S, X155L, X156Q, X215G, X282V, and X284P; X42G, X54P, X150F, X152S, X155I, X156Q, X171I, X215G, and X241R; X42G, X54P, X150F, X152S, X155L, X156Q, X193M, and X215G; X42G, X54P, X150F, X152S, X155L, X156Q, X215G, X282V, and X284I; X42G, X54P, X150F, X152S, X155L, X156Q, X215G, and X283S; X42G, X54P, X150F, X152S, X155L, X156Q, X215G, and X284I; X42G, X54P, X150F, X152S, X155L, X156Y, and X215G.

2. The engineered polypeptide of Claim 1, in which the amino acid sequence further comprises one or more residue differences as compared to SEQ ID NO:2, selected from: X5K, X33L,

X36C, X41C/F/K/M/N/R, X42A/G, X44Q, X48D/E/G/K/T, X49T, X51K, X54P, X55L, X76S, X108V, X117G, X122F/Q, X126A, X148Q, X150A/F, X152S/T, X155A/I/K/L/T/V, X156Q/R/S, X160P, X164P, X165N, X182T, X215G/H/L, X218M, X241R, X267V, X270T, X273H, X325M, and X328I.

3. An engineered polypeptide having transaminase activity comprising an amino acid sequence having at least 80% sequence identity to reference sequence of SEQ ID NO:2 and

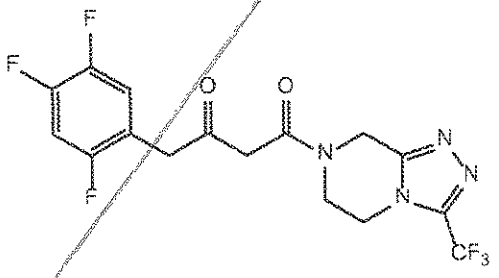
(a) an amino acid residue difference as compared to SEQ ID NO:2 selected from G36C, I41C, I41F, I41K, I41M, I41N, I41R, E42G, P48D, P48E, P48G, P48K, P48T, A51K, S54P, M122F, M122Q, Y148Q, C152T, Q155A, Q155I, Q155K, Q155T, Q155V, C215H, C215L, Y273H, L325M, and A241R; or

(b) a combination of residue differences selected from: A5K, E42G, S49T, S54P, C152S, Q155T, and W156Q; P33L, I41C, E42G, S54P, S150F, C152S, Q155K, F160P, and C215G; P33L, I41K, E42G, S54P, S150F, C152S, Q155I, F160P, and C215L; P33L, E42G, P48G, S54P, S150F, C152S, Q155T, and C215H; P33L, E42G, S54P, A109S, S150F, C152S, Q155K, W156Q, and C215H; P33L, E42G, S54P, E117G, S150F, C152S, Q155I, W156Q, and C215G; P33L, E42G, S54P, S150F, C152S, Q155I, W156Q, and C215G; P33L, E42G, S54P, S150F, C152S, Q155K, W156Q, and C215H; P33L, E42G, S54P, S150F, C152S, Q155L, W156Q, and C215H; P33L, E42G, S54P, S150F, C152S, Q155L, W156Q, C215H, and A241R; G36C, E42G, P48G, S54P, S150F, C152S, Q155I, and C215H; G36C, E42G, P48K, S54P, S150F, C152S, Q155T, and C215H; G36C, E42G, S54P, S150F, C152S, Q155I, C215H, and A241R; G36C, E42G, S54P, S150F, C152S, Q155K, C215H, and A241R; G36C, E42G, S54P, S150F, C152S, Q155T, and A241R; G36C, E42G, S54P, S150F, C152S, Q155V, and C215H; I41C, E42G, S49T, S54P, S150F, C152S, Q155I, F160P, C215G, and I267V; I41C, E42G, S49T, S54P, S150F, C152S, Q155K, W156Q, C215G and I267V; I41C, E42G, S54P, I108V, S150F, C152S, and Q155K; I41C, E42G, S54P, I108V, S150F, C152S, Q155K, W156Q, C215G, and I267V; I41C, E42G, S54P, I108V, S150F, C152S, Q155T, W156Q, and C215G; I41C, E42G, S54P, E117G, S150F, C152S, Q155K, and F160P; I41C, E42G, S54P, E117G, S150F, C152S, Q155K, and C215L; I41C, E42G, S54P, E117G, S150F, C152S, Q155L, and C215L; I41C, E42G, S54P, S150F, C152S, Q155I, and C215G; I41C, E42G, S54P, S150F, C152S, Q155I, and C215L; I41C, E42G, S54P, S150F, C152S, Q155K, W156Q, C215G, and I267V; I41C, E42G, S54P, S150F, C152S, Q155K, and C215L; I41C, E42G, S54P, S150F, C152S, Q155K, and C215G; I41C, E42G, S54P, S150F, C152S, Q155L, F160P, C215G, and I267V; I41C, E42G, S54P, S150F, C152S, Q155T, W156Q, F160P, and C215L; I41C, E42G, S54P, S150F, C152S, Q155T, W156Q, and C215L; I41F, E42G, S54P, M122Q, S150F, C152T, Q155V, W156Q, and C215G; I41F, E42G, S54P, S150F, C152S, Q155L, W156Q, V171I, and C215G; I41F, E42G, S54P, S150F, C152S, Q155L,W156Q,V171I, C215G, and A241R; I41F, E42G, S54P, S150F, C152S, Q155I, W156Q, and C215G; I41K, E42G, P48E, S54P, S150F, C152S, Q155K, and W156Q; I41K, E42G, P48E, S54P, S150F, C152S, Q155L, and C215L; I41K, E42G, S54P, I108V, E117G, S150F, C152S, Q155K, and C215L; I41K, E42G, S54P, I108V, S150F, C152S, Q155T, and

C215G; I41K, E42G, S54P, E117G, S150F, C152S, Q155L, and C215G; I41K, E42G, S54P, E117G, S150F, C152S, Q155K, C215L, and I267V; I41K, E42G, S54P, S150F, C152S, Q155K, W156Q, and C215G; I41K, E42G, S54P, S150F, C152S, Q155K, F160P, C215G, and I267V; I41K, E42G, S54P, S150F, C152S, Q155K, andC215L; I41K, E42G, S54P, S150F, C152S, and Q155T; I41K, E42G, S54P, S150F, C152S, Q155T, and F160P; I41K, E42G, S54P, S150F, C152S, Q155T, and C215G; I41K, E42G, S54P, S150F, C152S, Q155T, C215G, and I267V; I41K, E42G, S54P, S150F, C152S, Q155K, W156Q, and C215G; I41N, E42G, S54P, S150F, C152S, Q155I, and F160P; I41N, E42G, S54P, E117G, S150F, C152S, Q155T; and W156Q; I41N, S49T, E42G, S54P, S150F, C152S, Q155L, F160P, D165N, and C215L; E42A, A44Q, S54P, I108V, S150F, C152S, Q155T, and I267V; E42G, A44Q, S54P, I108V, S150F, C152S, and Q155T; E42G, A44Q, S54P, I108V, S150F, C152S, Q155T, and I267V; E42G, A44Q, S54P, S150A, C152S, and Q155T; E42G, A44Q, S54P, S150F, C152S, and Q155T; E42G, P48G, S54P, S150F, C152S, Q155L, W156Q, and C215H; E42G, P48G, S54P, S150F, C152S, and Q155T; E42G, S49T, S54P, I108V, E117G, S150F, C152S, Q155L, F160P, and C215L; E42G, S49T, S54P, I108V, E117G, S150F, C152S, Q155K, W156Q, and C215G; E42G, S49T, S54P, I108V, E117G, S150F, C152S, Q155T, W156Q, C215G, and I267V; E42G, S49T, S54P, C152S, Q155T, and W156Q; E42G, S54P, I55L, T126A, C152S, Q155T, L218M, and A270T; E42G, S54P, F60V, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, T68A, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, T69S, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, N76S, T126A, C152S, Q155T, S182T, L218M, A270T, and V328I; E42G, S54P, I108V, S150F, C152S, Q155K, and C215H; E42G, S54P, I108V, S150F, C152S, and Q155T; E42G, S54P, I108V, S150F, C152S, Q155T, and I267V; E42G, S54P, I108V, S150F, C152S, Q155V, W156Q, and F160P; E42G, S54P, E117G, C152S, and Q155T; E42G, S54P, E117G, C152S, Q155T, and W156Q; E42G, S54P, M122Q, S150F, C152S, Q155I, W156Q, C215G, and A241R; E42G, S54P, M122Q, S150F, C152S, Q155L,W156Q, V171I, C215G, and A241R; E42G, S54P, M122Q, S150F, C152T, Q155V, W156Q, V171I, C215G, and A241R; E42G, S54P, T126M, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, P135I, F136Y, S150F, C152S, Q155L, W156Q, W192F, and C215G; E42G, S54P, F136I, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, F136I, S150F, C152S, Q155L, W156Q, C215G, and G224I; E42G, S54P, F136I, S150F, C152S, Q155L, W156Y, C215G, S282V, and G284I; E42G, S54P, F136I, S150F, C152S, Q155L, W156Y, C215G, and G284P; E42G, S54P, F136Y, S150F, C152S, Q155L, W156Q, C215G, S282V, and G284P; E42G, S54P, S150A, C152S, Q155T, and I267V; E42G, S54P, S150F, C152S, Q155I, W156Q, F160P, C215L, and I267V; E42G, S54P, S150F, C152S, Q155I, W156Q, V171I, C215G, and A241R; E42G, S54P, S150F, C152S, Q155I, W156Q, and C215L; E42G, S54P, S150F, C152S, Q155I, F160P, and C215G; E42G, S54P, S150F, C152S, Q155I, and C215H; E42G, S54P, S150F, C152S, Q155K, and W156Q; E42G, S54P, S150F, C152S, Q155K, W156Q, and I267V; E42G, S54P, S150F, C152S, Q155L, W156Q, G193M, and C215G; E42G, S54P, S150F, C152S, Q155L, W156Q, and C215G; E42G, S54P, S150F, C152S, Q155L, W156Q, C215G, S282V, and G284I; E42G, S54P, S150F, C152S, Q155L, W156Q, C215G, and T283S; E42G, S54P, S150F, C152S, Q155L, W156Q, C215G, and G284I; E42G,

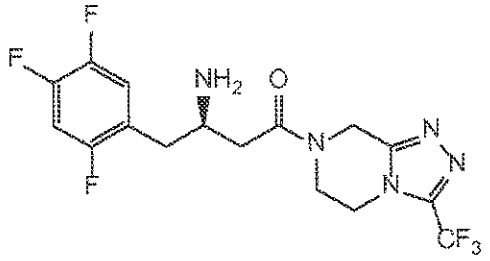
S54P, S150F, C152S, Q155L, W156Y, and C215G; E42G, S54P, S150F, C152S, Q155L, and C215H; E42G, S54P, S150F, C152S, and Q155T; E42G, S54P, S150F, C152S, Q155T, C215G, and I267V; E42G, S54P, S150F, C152S, Q155T, and I267V; E42G, S54P, S150F, C152S, Q155T, W156Q, F160P, C215L, and I267V; E42G, S54P, S150F, C152S, Q155T, W156Q, C215G, and I267V; E42G, S54P, S150F, C152S, Q155T, and W156R; E42G, S54P, S150F, C152S, Q155T, F160P, and C215G; E42G, S54P, S150F, C152S, Q155T, F160P, and C215L; E42G, S54P, S150F, C152S, Q155T, C215G, and I267V; E42G, S54P, S150F, C152S, Q155T, and I267V; E42G, S54P, C152S, Q155L, and W156S; E42G, S54P, C152S, Q155K, and W156S; E42G, S54P, C152S, Q155L, and W156S; E42G, S54P, C152S, and Q155T; E42G, S54P, C152S, Q155T, and F160P; E42G, S54P, C152S, Q155T, and R164P; E42G, S54P, C152S, Q155T, and W156Q; E42G, S54P, C152S, Q155T, and W156S; E42G, S54P, C152S, Q155T, and R164P; E42G, S54P,C152S, Q155T, S182T, L218M, and A270T; E42G, S54P, C152S, Q155T, and C215G; E42G, S54P, C152S, Q155T, and C215L; and E42G, S54P, C152S, Q155V, and W156S.

4. The engineered polypeptide of Claim 1, wherein said engineered polypeptide is capable of converting a substrate compound (**2**)



(**2**)

to a product compound (**1**)



(**1**)

under suitable reaction conditions.

5. The engineered polypeptide of Claim 4, which is capable of converting compound (**2**) to compound (**1**) with at least 1.2 fold the activity of SEQ ID NO:2 under suitable reaction conditions.

6. The engineered polypeptide of Claim 5, in which the suitable reaction conditions comprise compound (**2**) loading of at least 50 g/L, 1 mM PLP, 50% DMSO (v/v), 1.5 M isopropylamine, pH 11, and 55°C.

7. The engineered polypeptide of Claim 1, in which the amino acid sequence comprises a sequence selected from SEQ ID NO:4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38,40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254,256,258,260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, and 306.

8. The engineered polypeptide of Claim 1, in which the polypeptide is immobilized on a solid support.

9. The engineered polypeptide of Claim 8, in which the solid support is a bead or resin comprising polymethacrylate with epoxide functional groups, polymethacrylate with amino epoxide functional groups, styrene/DVB copolymer or polymethacrylate with octadecyl functional groups.

10. A polynucleotide encoding the engineered polypeptide of any one of Claims 1 to 7.

11. The polynucleotide of Claim 10, further comprising a nucleotide sequence selected from SEQ ID NO:3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 375, 277, 279, 281, 283, 285, 287, 291, 293, 295, 297, 299, 301, 303, and 305.

12. An expression vector comprising the polynucleotide of Claim 10 or 11.

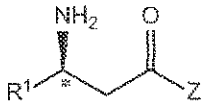
13. The expression vector of Claim 12, comprising at least one control sequence.

14. A host cell comprising the polynucleotide of Claim 10 or 11 or the expression vector of Claim 12 or 13.

15. A method of preparing the engineered polypeptide of any one of Claims 1 to 7, comprising culturing the host cell of Claim 14, under conditions suitable for expression of the polypeptide.

16. The method of Claim 15, further comprising isolating the polypeptide.

17. A process for preparing a compound of structural Formula (I):




(I)

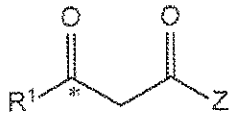
having the indicated stereochemical configuration at the stereogenic center marked with an *; in an enantiomeric excess of at least 70% over the opposite enantiomer,
wherein

Z is $OR^2$ or $NR^2R^3$;

$R^1$ is $C_{1-8}$ alkyl, aryl, heteroaryl, aryl-$C_{1-2}$ alkyl, heteroaryl-$C_{1-2}$ alkyl, or or a 5- to 6-membered heterocyclic ring system optionally containing an additional heteroatom selected from O, S, and N, the heterocyclic ring being unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, $C_{1-4}$ alkoxy, and $C_{1-4}$ alkyl, wherein alkyl and alkoxy are unsubstituted or substituted with one to five fluorines;

$R^2$ and $R^3$ are each independently hydrogen, $C_{1-8}$ alkyl, aryl, or aryl-$C_{1-2}$ alkyl; or

$R^2$ and $R^3$ together with the nitrogen atom to which they are attached form a 4- to 7-membered heterocyclic ring system optionally containing an additional heteroatom selected from O, S, and N, the heterocyclic ring being unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, $C_{1-4}$ alkoxy, and $C_{1-4}$ alkyl, wherein alkyl and alkoxy are unsubstituted or substituted with one to five fluorines; and the heterocyclic ring system being optionally fused with a 5- to 6-membered saturated or aromatic carbocyclic ring system or a 5- to 6-membered saturated or aromatic heterocyclic ring system containing one to two heteroatoms selected from O, S, and N, the fused ring system being unsubstituted or substituted with one to two substituents selected from hydroxy, amino, fluorine, $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy, and trifluoromethyl; the process comprising the step of contacting a compound of structural Formula (II):



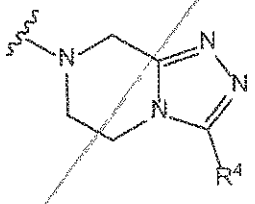
(II)

with an engineered polypeptide of any one of Claims 1 to 9 in the presence of an amino group donor in a suitable organic solvent under suitable reaction conditions.

18. The process of Claim 17, wherein $R^1$ is benzyl wherein the phenyl group of benzyl is unsubstituted or substituted one to three substituents selected from the group consisting of fluorine, trifluoromethyl, and trifluoromethoxy.

19. The process of Claim 17, wherein Z is $NR^2R^3$.

20. The process of Claim 19, wherein $NR^2R^3$ is a heterocycle of the structural Formula (III):

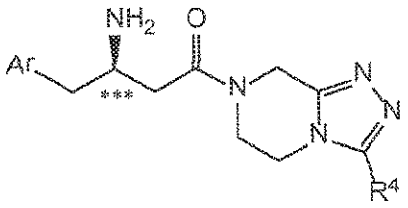


(III)

wherein $R^4$ is hydrogen or $C_{1-4}$ alkyl which is unsubstituted or substituted with one to five fluorines.

21. The process of any one of Claims 17 to 20, wherein the compound of structural Formula (II) excludes compound (2) and the compound of structural Formula (I) excludes compound (1).

22. A process for preparing a compound of structural Formula (Ia):



(Ia)

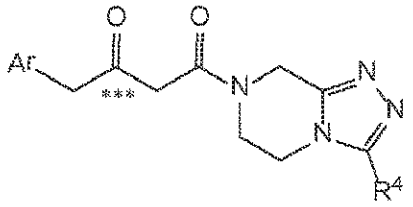
having the (*R*)-configuration at the stereogenic center marked with an ***; in an enantiomeric excess of at least 70% over the enantiomer having the opposite (*S*)-configuration;

wherein,

Ar is phenyl which is unsubstituted or substituted with one to five substituents independently selected from the group consisting of fluorine, trifluoromethyl, and trifluoromethoxy; and

$R^4$ is hydrogen or $C_{1-4}$ alkyl unsubstituted or substituted with one to five fluorines; the process comprising the step of:

contacting a prochiral ketone of structural Formula **(IIa)**:



**(IIa)**

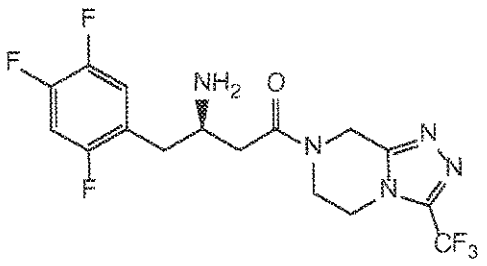
with an engineered polypeptide of any one of Claims 1 to 9, in the presence of an amino group donor under suitable reaction conditions.

23. The process of Claim 22, wherein Ar is 2,5-difluorophenyl or 2,4,5-trifluorophenyl and $R^4$ is trifluoromethyl.

24. The process of Claim 23, wherein Ar is 2,4,5-trifluorophenyl.

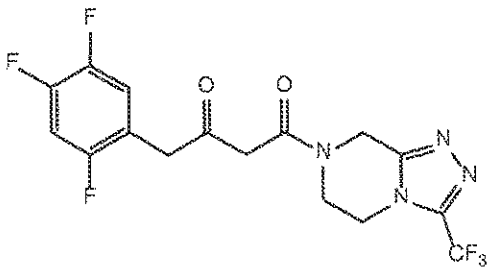
25. The process of any one of Claims 22 to 24, wherein the compound of structural Formula (**IIa**) exclude compound **(2)** and the compound of structural Formula (**Ia**) excludes compound **(1)**.

26. A process of preparing compound **(1)**



**(1)**

comprising a step of contacting a substrate of compound **(2)**



(2)

with an engineered polypeptide of any one of Claims 1 to 9, in the presence of an amino group donor under suitable reaction conditions.

27. The process of any one of Claims 17 to 26, wherein the compound of Formula (I), the compound of Formula (Ia), or the compound (1) is produced in at least 90% enantiomeric excess.

28. The process of any one of Claims 17 to 26, wherein the compound of Formula (I), the compound of Formula (Ia), or the compound (1) is produced in at least 99% enantiomeric excess.

29. The process of any one of Claims 17 to 26, wherein the amino group donor is selected from isopropylamine, alanine, 3-aminobutyric acid, or methylbenzylamine.

30. The process of Claim 29, wherein the amino group donor is isopropylamine, optionally at a concentration of about 0.1 to about 3.0 M, 0.2 to about 2.5 M, about 0.5 to about 2 M or about 1 to about 2 M.

31. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise a pH of from about pH 9.5 to about pH 11.5.

32. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise a temperature of about 45°C to about 60°C.

33. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise dimethylsulfoxide (DMSO) at about 30% (v/v) to about 60% (v/v).

34. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise the substrate compound at a loading of about 5 g/L to about 200 g/L, about 10 g/L to about 150 g/L, or about 50 g/L to about 100 g/L.

35. The process of any one of Claims 17 to 26, wherein the suitable reaction conditions comprise the engineered polypeptide at a concentration of from about 0.5 g/L to about 5 g/L, about 0.5 g/L to about 3 g/L, about 0.5 g/L to about 2 g/L, or from about 0.5 g/L to about 1 g/L.

36. The process of Claim 26, wherein the suitable reaction conditions comprise: (a) substrate loading of about 10 to 200 g/L of substrate compound **(2)**; (b) engineered polypeptide concentration of about 0.5 g/L to 5 g/L; (c) IPM concentration of about 0.1 to 3 M; (d) PLP cofactor concentration of about 0.1 to 1 mM; (e) DMSO concentration of about 30% (v/v) to about 60% (v/v); (f) pH of about 9.5 to 11.5; and (g) temperature of about 45°C to 60°C.

37. The process of Claim 26, wherein the suitable reaction conditions comprise: (a) about 50 g/L of substrate compound **(2)**; (b) about 2 g/L engineered polypeptide; (c) about 50% (v/v) dimethylsulfoxide (DMSO); (d) about 1 M isopropylamine (IPM); (e) about 1 mM pyridoxal phosphate (PLP); (f) about pH 10; and (g) about 50°C.

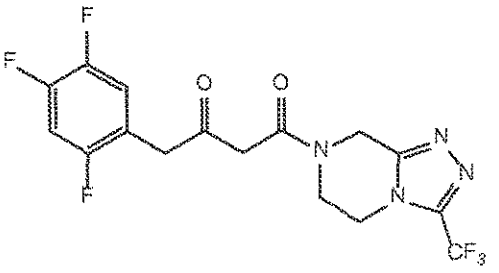
38. The process of any one of Claims 17 to 26, further comprising the step of isolating the compound of Formula **(I)**, the compound of Formula **(Ia)**, or the compound **(1)** from the reaction.

39. The process of any one of Claims 17 to 26, further comprising the step of converting the compound of Formula **(Ia)**, or the compound **(1)** into a pharmaceutically acceptable salt by contacting said compound with a pharmaceutically acceptable acid in a suitable reaction solvent.

40. The process of Claim 39, wherein the pharmaceutically acceptable acid is phosphoric acid and the pharmaceutically acceptable salt is the dihydrogen phosphate salt.

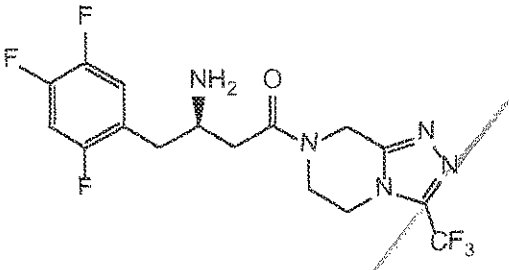
41. The process of Claim 40, further comprising the step of crystallizing the pharmaceutically acceptable salt from the reaction solvent.

42. A process for the preparation of (2*R*)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-*a*]pyrazin-7(8*H*)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine phosphate (1:1) monohydrate, the process comprising a step of converting a substrate compound (**2**)



(2)

to a product compound (1)



(1)

by contacting a substrate of compound (2) with an engineered polypeptide of any one of Claims 1 to 9, in the presence of an amino group donor under suitable reaction conditions.

43. The method of Claim 42, in which the amino group donor is isopropylamine.