In one aspect, provided herein is a polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1, wherein

(a) residue 467 is Ser, residue 267 is Glu, and residue 271 is Asp; and

(b) the polypeptide comprises an amino acid change from SEQ ID NO: 1 at one or more residues selected from the group consisting of 221D/N/Q/H, 262E, 268S/T/A, 269L/T, 270A/T/V, 319A, 320M, 354A/E/Q/R/Y, 358N/S/Q/T, 368F/Q, 399Q, 402S/Q, 406S, 424K, 449E/N/Q, 461R, and 463A/L/M/Q/R/T/V, wherein the polypeptide has an improved gliadin endopeptidase activity over a polypeptide having the amino acid sequence set forth in SEQ ID NO: 1.

In another aspect, provided herein is a polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 71, wherein

(a) residue 278 is Ser, residue 78 is Glu, and residue 82 is Asp; and

(b) the polypeptide comprises an amino acid change from SEQ ID NO: 71 at one or more residues selected from the group consisting of 32D/N/Q/H, 73E, 79S/T/A, 80L/T, 81A/T/V, 130A, 131M, 165E/Q/R/Y, 169S/Q/T, 179F/Q, 210Q, 213S/Q, 217S, 235K, 260E/N/Q, 272R, and 274A/L/M/Q/R/T/V, wherein the polypeptide has an improved gliadin endopeptidase activity over a polypeptide having an amino acid sequence set forth in SEQ ID NO: 71.

In another aspect, provided herein is a polypeptide comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 59, wherein

(a) residue 467 is Ser, residue 267 is Glu, and residue 271 is Asp; and

(b) the polypeptide comprises amino acids 262E, 269T, 320M, 354Q, 358S, 399Q, 449Q, and 463T.

In another aspect, provided herein is a nucleic acid encoding the polypeptide described herein.

In another aspect, provided herein is a nucleic acid expression vector comprising the isolated nucleic acid described herein.

In another aspect, provided herein is a recombinant host cell comprising the nucleic acid expression vector described herein.

In another aspect, provided herein is a pharmaceutical composition, comprising a polypeptide described herein, the nucleic acid described herein, the nucleic acid expression vector described herein, and/or the recombinant host cell described herein, and a pharmaceutically acceptable carrier.

In another aspect, provided herein is the use of a polypeptide described herein or the pharmaceutical composition described herein in the manufacture of a medicament for treating celiac sprue or non-celiac gluten sensitivity (NCGS), wherein an effective amount of the polypeptide or the pharmaceutical composition to treat the celiac sprue or NCGS is to be administered to an individual with celiac sprue or NCGS.

In another aspect, provided herein is a polypeptide described herein or the pharmaceutical composition described herein for use in therapy.

In one aspect, the invention provides polypeptides comprising an amino acid sequence at least 75%, 80%, 85%, 90%, 95%, or more identical to the amino acid sequence of SEQ ID NO: 1, wherein

(a) residue 467 is Ser, residue 267 is Glu, and residue 271 is Asp; and

(b) the polypeptide comprises an amino acid change from SEQ ID NO: 1 at one or more residues selected from the group consisting of 463, 221, 262E, 268, 269, 270, 319A, 320, 354E/Q/R/Y, 358S/Q/T, 368F/Q, 399, 402, 406, 424, 449, 461, 105, 171, 172, 173, 174, and 456.

In one embodiment, the polypeptide comprises an amino acid change from SEQ ID NO: 1 at one or more residues selected from the group consisting of 463, 221, 262E, 268, 269, 270, 319A, 320, 354E/Q/R/Y, 358S/Q/T, 368F/Q, 399, 402, 406, 424, 449, and 461. In another embodiment, the polypeptide comprises an amino acid change from SEQ ID NO: 1 at one or more residues selected from the group consisting of 221D/N/Q/H, 262E, 268S/T/A, 269L/T, 270A/T/V, 319A, 354E/Q/R/Y, 358S/Q/T, 368F/Q, 399Q, 402S/Q, 406S, 424K, 449E/N/Q, 461R, and 463A/L/M/Q/R/T/V. In a further embodiment, the polypeptide comprises an amino acid change from SEQ ID NO: 1 at 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or more residues selected from the group.

In one embodiment, the polypeptide comprises amino acid changes from SEQ ID NO: 1 at residues 399 and 449, such as amino acid changes 399Q and 449Q. In another embodiment, the polypeptide comprises amino acid changes 358S and 463T. In a further embodiment, the polypeptide comprises amino acid changes 262E, 269T, 354Q, 358S, 399Q, 449Q, and 463T. In another embodiment, the polypeptide comprises amino acid changes 319A, 368F, 399Q, 449Q, and 463T. In a further embodiment, the polypeptide comprises amino acid changes 262E, 269T, 270V, 354Q, 358S, 399Q, and 449Q. In a still further embodiment, the polypeptide comprises amino acid changes 262E, 269T, 320M, 354Q, 358S, 399Q, 449Q, and 463T. In another embodiment, the polypeptide comprises amino acid changes 319A, 320M, 368F, 399Q, 449Q, and 463T. In one embodiment, the polypeptides

comprise an amino acid change from SEQ ID NO: 1 at one or more amino acid positions selected from the group consisting of 105, 171, 172, 173, 174, and 456, such as amino acid changes 105H; 171R A, or S; 172R, A, or S; 173R or S, 174S, and/or 456V.

In another aspect, the invention provides polypeptide comprising an amino acid sequence at least 75%, 80%, 85%, 90%, 95%, or more identical to the amino acid sequence of SEQ ID NO: 71, wherein

(a) residue 278 is Ser, residue 78 is Glu, and residue 82 is Asp; and