BRIEF SUMMARY

Certain embodiments relate to an isolated arginine deiminase, wherein the isolated arginine deiminase has reduced cross-reactivity with patient anti-ADI-PEG 20 antibodies. Also included are therapeutic or pharmaceutical compositions comprising an isolated arginine deiminase or a fragment thereof having ADI activity, and a pharmaceutically-acceptable carrier. In certain embodiments, the composition is sterile and/or substantially free of pyrogens such as endotoxins. In some embodiments, the isolated arginine deiminase having reduced cross-reactivity with patient anti-ADI-PEG 20 antibodies is not from *M. hominis*. In some embodiments, the isolated arginine deiminase having reduced cross-reactivity with patient anti-ADI-PEG 20 antibodies is from an organism listed in Table 1.

In a first aspect of the present disclosure, there is provided a therapeutic composition comprising an isolated arginine deiminase, or a fragment thereof having arginine deiminase (ADI) activity, and a pharmaceutically-acceptable carrier, wherein the isolated arginine deiminase has reduced cross-reactivity with patient anti-ADI-PEG 20 antibodies and comprises the amino acid sequence set forth SEQ ID NO: 10, or a variant thereof that displays at least 90% sequence identity to SEQ ID NO:10.