

EXTENDED-RELEASE IMMUNE CELL ENGAGING PROTEINS AND METHODS OF TREATMENT

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/214,963, filed June 25, 2021; U.S. Provisional Patent Application No. 63/276,804, filed November 8, 2021; and U.S. Provisional Patent Application No. 63/328,603, filed April 7, 2022; each of which is incorporated herein by reference in its entirety.

INCORPORATION BY REFERENCE

[0002] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BACKGROUND

[0003] Cancer is the second leading cause of human death next to coronary disease. Worldwide, millions of people die from cancer every year. In the United States alone, cancer causes the death of well over a half-million people each year, with some 1.4 million new cases diagnosed per year. While deaths from heart disease have been declining significantly, those resulting from cancer generally are on the rise. In the early part of the next century, cancer is predicted to become the leading cause of death.

[0004] Moreover, even for those cancer patients that initially survive their primary cancers, common experience has shown that their lives are dramatically altered. Many cancer patients experience strong anxieties driven by the awareness of the potential for recurrence or treatment failure. Many cancer patients experience significant physical debilitations following treatment.

[0005] Generally speaking, the fundamental problem in the management of the deadliest cancers is the lack of effective and non-toxic systemic therapies. Cancer is a complex disease characterized by genetic mutations that lead to uncontrolled cell growth. Cancerous cells are present in all organisms and, under normal circumstances, their excessive growth is tightly regulated by various physiological factors. Controlling the toxicity of various cancer therapies remain an important and unsolved issue.

SUMMARY OF THE INVENTION

[0005a] Provided herein is a pharmaceutical composition comprising an extended-release binding protein, wherein the extended-release binding protein comprises a half-life extended immune cell engaging protein, a masking peptide, and a cleavable linker; wherein the half-life

extended immune cell engaging protein comprises a first domain (A), a second domain (B), and a third domain (C), wherein: (i) the first domain (A) comprises an immune cell engaging domain, (ii) the second domain (B) comprises a half-life extended domain, and (iii) the third domain (C) specifically binds to a target antigen; wherein the cleavable linker covalently links the masking peptide to the N-terminus or the C-terminus of the half-life-extended immune cell engaging protein, and wherein the cleavable linker is significantly cleaved in systemic circulation.

[0006] Provided here in is a pharmaceutical composition comprising an extended-release binding protein which comprises a half-life extended immune cell engaging protein, a masking peptide, and a cleavable linker, wherein the masking peptide is covalently linked to the N-