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(54) **HIGH-AFFINITY MONOCLONAL ANTIBODIES TO GLYPICAN-3 AND USE THEREOF**

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(58) **Field of Classification Search**

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See application file for complete search history.

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(57) **ABSTRACT**

Described herein is the identification of a panel of high affinity monoclonal antibodies that bind GPC3. The disclosed antibodies recognize native GPC3 on the surface of cancer cells, as well as soluble GPC3. The highest affinity antibody (YP7) was further characterized and shown to be highly sensitive in that it was capable of detecting cancer cells with low expression of GPC3. YP7 also exhibited significant HCC tumor growth inhibition in vivo. Immunotoxins comprising the antibodies disclosed herein fused to PE38 exhibited very high binding affinity for GPC3-expressing cells and significantly inhibited GPC3-expressing cancer cell growth. Thus, the high-affinity monoclonal antibodies disclosed herein can be used for the diagnosis and treatment of GPC3-expressing cancers.

33 Claims, 23 Drawing Sheets