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(71) Applicant: **REGENERON PHARMACEUTICALS, INC.** [US/US]; 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US).

(72) Inventors: **EGERMAN, Marc**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **PHAN, Chauhongduc**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **WANG, Ni-anshuang**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **SHEN, Yang**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **WANG, Xin**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **DEVALARAJA-NARASHIMHA, Kishor**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **GLASS, David**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US).

(74) Agent: **BRUNER, J. Kyle** et al.; BIOSPARK INTELLECTUAL PROPERTY LAW, 1 Broadway, 14th Floor, Cambridge, Massachusetts 02142 (US).

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(54) Title: ENGINEERED ALPHA KLOTHO POLYPEPTIDES AND USES THEREOF

(57) Abstract: The present disclosure provides engineered alpha klotho polypeptides and methods of their production and use. Soluble alpha klotho polypeptides disclosed herein comprise an alpha klotho moiety having one or more mutations for enhancing activity, production yield, and/or stability relative to human alpha klotho. The disclosure further provides pharmaceutical compositions comprising the engineered alpha klotho polypeptides, and methods of use of the engineered alpha klotho polypeptides in treatment methods, including treatment of age-related conditions and kidney disease. Also disclosed are nucleic acids encoding the engineered alpha klotho polypeptides, recombinant cells that express the engineered alpha klotho polypeptides, and methods of producing the engineered alpha klotho polypeptides.