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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government Owned Inventions Available for Licensing or Collaboration: RFXP1

AGONISTS

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The National Center for Advancing Translational Sciences (NCATS), an institute of the National Institutes of Health (NIH), Department of Health and Human Services (HHS), is giving notice of the licensing opportunities for the inventions listed below, which are owned by an agency of the U.S. Government, Florida International University (FIU), and University of South Florida (USF). The NCATS has taken the lead in both patenting and licensing via consolidation of rights under an Inter Institutional Agreement (IIA). The inventions are available for licensing and collaboration to achieve expeditious commercialization results of federally funded research and development.

FOR FURTHER INFORMATION CONTACT: Inquiries related to these licensing or collaboration opportunities should be directed to: Jasmine Kalsi, M.S., Licensing and Patenting Manager, Office of Strategic Alliances (OSA), NCATS, Email: *jasmine.kalsi@nih.gov* or Phone: 301-435-0129. Respondents will be required to submit an ‘‘Application for License to Public Health Service Inventions.’’ An executed CDA will be required to receive copies of the patent applications.

SUPPLEMENTARY INFORMATION:

NIH seeks to ensure that technologies developed by NIH and its partners are expeditiously commercialized and brought to practical use. NCATS is actively seeking a licensing partner to

facilitate the development and commercialization of a technology or small molecule compounds that are in an early phase of development for therapeutic interventions for cancers, fibrotic and vascular disease including but not limited to breast cancer, solid tumors, atherosclerosis, and liver fibrosis.

NCATS in collaboration with Florida International University (FIU) and University of South Florida (USF) has identified low molecular weight, highly potent, and efficient full RXFP1 agonists with low cytotoxicity. The identification and characterization of these compounds may lead to the development of a new class of cost-effective drugs for the treatment of numerous cancers, fibrotic, and vascular disorders.

It is well documented in literature that activation of RXFP1 by relaxin induces: 1) up-regulation of the endothelin system which leads to vasodilation; 2) extracellular matrix remodeling through regulation of collagen deposition, cell invasiveness, proliferation, and overall tissue homeostasis; 3) a moderation of inflammation by reducing levels of inflammatory cytokines, such as TNF-a and TGF-b; and 4) angiogenesis by activating transcription of VEGF.

The present invention is directed to novel relaxin receptor (RFXP1 receptor) small molecule agonists useful for treating relaxin-related disorders including fibrosis, certain cancers, vascular calcifications, including atherosclerosis, and heart failure. The RFXP1 agonists of this invention possess a number of advantages not found in earlier RFXP1 agonists. These properties include, for example, improved bioavailability, low toxicity, and better activity in RXFP1-dependent biological functional assays.

The development of small-molecule agonists of RXFP1 would have numerous benefits and will allow investigating additional therapeutic applications where chronic administration is required. NCATS has identified a series of small-molecule agonists of RXFP1 which are potent, highly selective, easy to synthesize, and with reasonable metabolic and physical properties. Our molecules display similar efficacy as the natural hormone in several functional assays. Mutagenesis studies have mapped the specific regions responsible for relaxin receptor activation

by these compounds to an allosteric site on the receptor. Finally, these compounds display good in vivo pharmacokinetic properties and are currently being evaluated in vivo.

This Notice is in accordance with 35 U.S.C. 209 and 37 CFR Part 404.

NIH Reference Number: E-145-2024-0.

Product Type: Therapeutics.

Therapeutic Area(s): Reproductive Health, Pulmonology, Oncology, Geriatrics, Dermatology, Cardiology.

Potential Commercial Applications:

- Vascular health
- Fibrotic diseases
- Cancers
- Human reproductive health

Competitive Advantages:

- Potent and highly selective
- Bioavailable with excellent exposure
- Easy to synthesize and scale-up

Publication:

"Anti-apoptotic and Matrix Remodeling Actions of a Small Molecule Agonist of the Human Relaxin Receptor, ML290 in Mice With Unilateral Ureteral Obstruction." Ng HH, Soula M, Rivas B, Wilson KJ, Marugan JJ, Agoulnik AI. Front Physiol. 2021 Jul 7.

Therapeutic effects of a small molecule agonist of the relaxin receptor ML290 in liver fibrosis. Kaftanovskaya EM, Ng HH, Soula M, Rivas B, Myhr C, Ho BA, Cervantes BA, Shupe TD, Devarasetty M, Hu X, Xu X, Patnaik S, Wilson KJ, Barnaeva E, Ferrer M, Southall NT, Marugan JJ, Bishop CE, Agoulnik IU, Agoulnik AI. FASEB J. 2019 Nov

Optimization of the first small-molecule relaxin/insulin-like family peptide receptor (RXFP1) agonists: Activation results in an antifibrotic gene expression profile.

Wilson KJ, Xiao J, Chen CZ, Huang Z, Agoulnik IU, Ferrer M, Southall N, Hu X, Zheng W, Xu X, Wang A, Myhr C, Barnaeva E, George ER, Agoulnik AI, Marugan JJ. Eur J Med Chem. 2018 Aug 5

ML290 is a biased allosteric agonist at the relaxin receptor RXFP1. Kocan M, Sarwar M, Ang SY, Xiao J, Marugan JJ, Hossain MA, Wang C, Hutchinson DS, Samuel CS, Agoulnik AI, Bathgate RAD, Summers RJ. Sci Rep. 2017 Jun 7

Structural Insights into the Activation of Human Relaxin Family Peptide Receptor 1 by Small-Molecule Agonists. Hu X, Myhr C, Huang Z, Xiao J, Barnaeva E, Ho BA, Agoulnik IU, Ferrer M, Marugan JJ, Southall N, Agoulnik AI. Biochemistry. 2016 Mar 29

Activation of Relaxin Family Receptor 1 from Different Mammalian Species by Relaxin Peptide and Small-Molecule Agonist ML290. Huang Z, Myhr C, Bathgate RA, Ho BA, Bueno A, Hu X, Xiao J, Southall N, Barnaeva E, Agoulnik IU, Marugan JJ, Ferrer M, Agoulnik AI. Front Endocrinol (Lausanne). 2015 Aug 17

Identification and optimization of small-molecule agonists of the human relaxin hormone receptor RXFP1. Xiao J, Huang Z, Chen CZ, Agoulnik IU, Southall N, Hu X, Jones RE, Ferrer M, Zheng W, Agoulnik AI, Marugan JJ. Nat Commun. 2013

Discovery, optimization, and biological activity of the first potent and selective small-molecule agonist series of human relaxin receptor 1 (RXFP1). Xiao J, Chen CZ, Huang Z, Agoulnik IU, Ferrer M, Southall N, Hu X, Zheng W, Agoulnik AI, Marugan JJ. 2012 Mar 10 [updated 2013 May 8]

Identification of small-molecule agonists of human relaxin family receptor 1 (RXFP1) by using a homogenous cell-based cAMP assay. Chen CZ, Southall N, Xiao J, Marugan JJ, Ferrer M, Hu X, Jones RE, Feng S, Agoulnik IU, Zheng W, Agoulnik AI. J Biomol Screen. 2013 Jul

Patent Status: RFXP1 AGONISTS," U.S. Provisional Application No. 63/780,976 and NIH Reference No.: E-145-2024-0-US-02 filed 31 March 2025

Development Stage: Preclinical (in vitro).

Date: August 20, 2025

Joni L. Rutter,

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National Center for Advancing Translational Sciences

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