



Karuna Receives Wellcome Trust Award to Advance Innovative Clinical Stage Product Candidate for the Treatment of Schizophrenia

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Karuna Pharmaceuticals, Inc. ("Karuna", a PureTech Health plc (PureTech, PRTC.L) operating company) announces receipt of a Translation Fund Award from the Wellcome Trust of up to \$3.84 million. Additionally, PureTech is investing a further \$1.5 million in Karuna. The funding will be applied to further develop Karuna's lead program, KarXT, a potentially innovative therapy for the treatment of schizophrenia.

Daphne Zohar, Chief Executive Officer of PureTech, said: "We are honored by the support of the Wellcome Trust and the recognition of the potential of Karuna's KarXT program as a potentially ground breaking new approach for treating schizophrenia. This award, recognizing the important work of Karuna, provides further external validation of our approach and the potential to have an impact on patient's lives."

Karuna Receives Wellcome Trust Award to Advance Innovative Clinical Stage Product Candidate for the Treatment of Schizophrenia

Boston, August 5, 2015 – Karuna Pharmaceuticals, Inc. ("Karuna"), a PureTech (PureTech Health plc PRTC.L) company developing a novel product candidate for the treatment of schizophrenia, announced today that it has received a Translation Fund Award from the Wellcome Trust comprising an unsecured convertible loan to Karuna of up to \$3.84 million. The funding, along with other capital, will be applied to further develop Karuna's lead program KarXT, a potentially innovative therapy for the treatment of schizophrenia.

Schizophrenia is a severe and chronic mental health disorder that affects more than 21 million people worldwide. The disease is characterized by profound disruptions in thinking, affecting language, perception, and the sense of self, that typically includes psychotic episodes. Antipsychotics are the mainstay therapy for the treatment of schizophrenia. However, significant unmet need remains due to the limited efficacy and potential serious side effects associated with current antipsychotic medications.

"Few safe and effective new mechanisms for therapy of schizophrenia have emerged over the last half-century, and we believe that Karuna's novel approach has the potential to change the treatment paradigm in the field," said Dr. Ben Shapiro, Non-Executive Director of Karuna and PureTech and formerly Executive Vice President of Merck Research Laboratories. "We are delighted that the Wellcome Trust is supporting the development of this potentially important new therapy for schizophrenia, a disease that has a devastating impact on the lives of patients and their loved ones."

KarXT selectively targets the muscarinic system and is composed of xanomeline, a novel clinical-stage [muscarinic acetylcholine receptor](#) agonist (activator) and trospium chloride, an FDA-approved and well-established muscarinic receptor antagonist (blocker). The muscarinic system consists of five receptor subtypes that both bind acetylcholine and are widely distributed through the human body and have been linked to distinct physiological functions, including cognition.

Xanomeline has demonstrated efficacy in reducing psychosis and improving cognition in placebo-controlled human trials in both Alzheimer's disease and schizophrenia. In a double-blind, placebo-controlled monotherapy trial in schizophrenia patients, a significant 24-point reduction over placebo was observed in the Positive and Negative Symptom Scale.

While xanomeline alone has displayed strong efficacy, it has side effects associated with binding receptors outside the central nervous system, limiting its therapeutic utility. Karuna believes that the addition of trospium chloride may reduce the side effects typically seen with xanomeline alone. As a muscarinic antagonist (blocker), trospium chloride could potentially inhibit xanomeline's binding to peripheral receptors, and therefore improve xanomeline's safety profile. At the same time, since it has been shown that trospium chloride does not enter the central nervous system, we expect that it would not inhibit xanomeline's binding to muscarinic receptors in the brain. Karuna has a worldwide exclusive license for xanomeline, as detailed in PureTech's IPO prospectus published on 19 June 2015, and has a patent portfolio more broadly covering selective muscarinic targeting enabled by the KarXT approach.

Karuna plans to conduct a safety proof of concept study in 2016 to demonstrate that trospium chloride can improve xanomeline's tolerability profile, followed by a Phase II efficacy study of KarXT.

"The muscarinic system has shown enormous promise as a therapeutic target for the treatment of schizophrenia, but development efforts have been limited by tolerability concerns," said Alan Brier, M.D., Karuna's Chief Clinical Advisor and the former Chief Medical Officer at Eli Lilly. "The KarXT program has the potential to fulfill the long-held promise of therapeutics targeting muscarinic receptors."

PureTech, as part of its continued commitment to Karuna, is also investing an additional \$1.5 million to support the development of the KarXT program through its next milestone. PureTech has committed up to an additional \$17.5M to Karuna, pending the results of the next clinical trial which is fully funded.

About Wellcome Trust

The [Wellcome Trust](#) is a global charitable foundation dedicated to improving health. It provides more than £700 million a year to support bright minds in science, the humanities and the social sciences, as well as education, public engagement and the application of research to medicine. Its £18 billion investment portfolio gives us the independence to support such transformative work as the sequencing and understanding of the human genome, research that established front-line drugs for malaria, and Wellcome Collection, its free venue for the incurably curious that explores medicine, life and art. www.wellcome.ac.uk

About Wellcome Trust Translation Fund Awards

The aim of Wellcome Trust Translation Awards is to develop innovative and ground breaking new technologies in the biomedical area. Projects must

have already demonstrated proof of principle, supported by experimental data. Applications should bridge the funding gap in commercialization of new technologies in the biomedical area and must plan to take the product, technology or intervention to a stage at which it is sufficiently developed to be attractive to another party.

About Karuna

Karuna is a clinical-stage drug development company pursuing innovative therapies for the treatment of schizophrenia. Karuna's lead program, KarXT, is a product candidate consisting of xanomeline, a novel clinical-stage [muscarinic acetylcholine receptor](#) agonist (activator) that has demonstrated efficacy in reducing psychosis and improving cognition in placebo-controlled human trials, and trospium chloride, an FDA-approved and well-established muscarinic receptor antagonist (blocker) that studies have shown does not enter the central nervous system. For more information, visit www.karunapharma.com.

About PureTech

PureTech (PureTech Health plc, PRTC.L) is a science-driven healthcare company, seeking to solve some of today's toughest health challenges through disruptive approaches. Based in Boston, Massachusetts, PureTech has a pipeline of 12 operating companies, seven of which are "growth stage" with external validation including strategic partnerships, outside funding, proof-of-concept or peer review in prestigious scientific journals. PureTech is problem-focused and solution-agnostic, looking beyond traditional disciplines and approaching healthcare problems from different perspectives. Focusing on areas of significant unmet medical need, PureTech evaluates more than 650 ideas per year, prioritizing, selecting and testing what it believes to be the most scientifically and commercially promising concepts to advance. PureTech's leading team and board, along with an advisory network of more than 50 experts across multiple disciplines, gives PureTech access to potentially groundbreaking science and technological innovations. For more information, visit www.puretechhealth.com and connect with us on [Twitter](#).

PureTech has holdings of 81.5% in Karuna on a diluted basis, and is entitled to a royalty on net sales of KarXT. This calculation of PureTech's holding includes issued and outstanding shares as well as options to purchase shares, but excludes unallocated shares authorised to be issued pursuant to equity incentive plans and any shares issuable upon conversion of outstanding convertible promissory notes.

PureTech Forward-Looking Statement

This press release contains statements that are or may be forward-looking statements, including statements that relate to the company's future prospects, developments and strategies. The forward-looking statements are based on current expectations and are subject to known and unknown risks and uncertainties that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, those risks and uncertainties described in the risk factors included in the company's regulatory filings. These forward-looking statements are based on assumptions regarding the present and future business strategies of the company and the environment in which it will operate in the future. Each forward-looking statement speaks only as at the date of this press release. Except as required by law, regulatory requirement, the Listing Rules and the Disclosure and Transparency Rules, neither the company nor any other party intends to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.