



PureTech's Karuna Receives \$8 Million Wellcome Trust Award to Advance Phase 2 Product Candidate for the Treatment of Schizophrenia

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Karuna's proprietary approach leverages novel mechanism to treat psychosis and cognition in mental health conditions

PureTech Health plc (LSE: PRTC) ("PureTech Health"), an advanced, clinical-stage biopharmaceutical company, today announced that its affiliate, Karuna, has received a Translational Fund Award from the Wellcome Trust for approximately \$8 million. The funding will be used to advance Karuna's lead product candidate KarXT through a Phase 2 study in people with schizophrenia.

Eric Elenko PhD, Chief of Research and Strategy at PureTech Health, said: "This award from Wellcome acknowledges Karuna's first-in-class approach to address CNS illnesses with tremendous unmet need. We are well-positioned to continue to advance this promising new treatment for schizophrenia, a debilitating disease that affects over 20 million people, and we look forward to potentially expanding across other CNS disorders.

Wellcome previously awarded Karuna \$3.8 million to fund a Phase 1 tolerability proof-of-concept study with KarXT, which reported successful results. Both awards have been structured in the form of unsecured convertible loans.

The full text of the announcement from Karuna is as follows:

Karuna Receives \$8 Million Wellcome Trust Award to Advance First-in-Class Phase 2 Clinical Programme in Schizophrenia

Karuna's proprietary approach leverages novel mechanism to treat psychosis and cognition in mental health conditions

BOSTON, June 19, 2018 —[Karuna Pharmaceuticals](#), an affiliate of [PureTech Health plc](#) (LSE: PRTC), focused on targeting muscarinic receptors for the treatment of disorders marked by psychosis and cognitive symptoms, today announced that it has been awarded approximately \$8 million by the Wellcome Trust. The funding will be used to further advance clinical development of Karuna's lead programme, KarXT (Karuna-Xanomeline-Trospium), through a Phase 2 study in people with schizophrenia.

"Antipsychotics are the mainstay therapy for the treatment of schizophrenia and have all relied on the same fundamental mechanism of action for the past 60 years. Currently available treatments have limited efficacy – primarily addressing only positive symptoms, such as hallucinations and delusions – and are often associated with serious, often irreversible, side effects, leaving a significant need for new treatments for people living with this devastating disease," said Andrew Miller, PhD, President and Chief Executive Officer of Karuna. "With KarXT, we have an opportunity to potentially improve positive, negative, and cognitive symptoms based on prior compelling efficacy data with xanomeline, and without the debilitating side effects of existing therapies. We are delighted that Wellcome is continuing to back this important new therapeutic approach."

Xanomeline previously demonstrated compelling efficacy in double-blind placebo-controlled studies in schizophrenia and Alzheimer's disease; at that time tolerability issues associated with the activation of muscarinic receptors outside the brain hindered xanomeline's further development. Karuna's KarXT is designed to improve tolerability and unlock the potential of muscarinic agonists by selectively targeting M1/M4 muscarinic receptors in the brain while blocking their activation in tissues outside the brain. KarXT has demonstrated a significant improvement in tolerability compared to xanomeline in a double-blind, placebo-controlled, healthy volunteer study, and Karuna is currently completing a Phase 1 study using a proprietary co-formulation of xanomeline and trospium. The Phase 2 acute psychosis trial in people with schizophrenia is designed to replicate and expand on the previous efficacy results with xanomeline and is expected to begin in the third quarter of 2018.

Dr Lynsey Bilsland, from Wellcome's Innovations team said: "Karuna's treatment candidate has the potential to have a significant impact on patients affected by schizophrenia and other psychotic disorders. Research in this important area has long been under-resourced, and doctors and patients currently rely on treatments which have existed for decades. Wellcome is committed to supporting the innovation vital to developing global understanding and treatment of mental illness and improving life for patients affected."

Wellcome previously awarded Karuna \$3.8 million to fund a Phase 1 tolerability proof-of-concept study with KarXT, which reported successful results. Both awards have been structured in the form of unsecured convertible loans.

About Schizophrenia

Schizophrenia affects more than 20 million people worldwide and is characterised by profound disruptions to daily life. Symptoms are grouped within three domains: positive, negative, and cognitive. Positive symptoms are generally associated with psychotic behaviours, including hallucinations and delusions. Negative symptoms refer to disruptions in behaviour and emotions and can manifest as reduced social engagement and motivation. Cognitive symptoms are marked by changes in memory and attention. The prognosis for schizophrenia remains poor as 30 percent of patients live independently and only 10 to 20 percent maintain full-time employment. There is a desperate need for new treatments in schizophrenia that not only address positive, negative, and cognitive symptoms of the disease, but are also safer than existing medicines.

About Wellcome

Wellcome exists to improve health for everyone by helping great ideas to thrive. We're a global charitable foundation, both politically and financially independent. We support scientists and researchers, take on big problems, fuel imaginations and spark debate.

About Karuna Pharmaceuticals

Karuna is a clinical-stage drug development company targeting muscarinic receptors for the treatment of psychosis and cognition across central nervous system (CNS) disorders, including schizophrenia and Alzheimer's disease. Karuna's lead product candidate, [KarXT](#), consists of xanomeline, a novel muscarinic acetylcholine receptor agonist that has demonstrated efficacy in placebo-controlled human trials in schizophrenia and Alzheimer's disease, and trospium chloride, an FDA-approved and well-established muscarinic receptor antagonist that has been shown not to enter the CNS. Karuna has demonstrated improved tolerability of KarXT vs xanomeline in a placebo-controlled human study and is currently conducting a Phase 1 study using a proprietary co-formulation of xanomeline and trospium. A Phase 2 trial of safety and efficacy in people with schizophrenia is expected to begin in the third quarter of 2018. Karuna, an affiliate of [PureTech Health](#) (LSE: PRTC), has a worldwide exclusive license for xanomeline and has a patent portfolio more broadly covering selective muscarinic targeting enabled by the KarXT approach. For more information, visit www.karunapharma.com.

About PureTech Health

PureTech Health (PRTC.L) is an advanced, clinical-stage biopharmaceutical company developing novel medicines targeting serious diseases that result from dysfunctions in the nervous, immune, and gastrointestinal systems (brain-immune-gut or the "BIG" axis), which together represent the adaptive human systems. PureTech Health is at the forefront of understanding and addressing the biological processes and crosstalk associated with the BIG axis. By harnessing this emerging field of human biology, PureTech Health is pioneering new categories of medicine with the potential to have great impact on people with serious diseases. PureTech Health is advancing a rich pipeline of innovative therapies that includes two pivotal stage programmes, multiple human proof-of-concept studies and a number of early clinical and pre-clinical programmes. PureTech's research and development pipeline has been advanced in collaboration with some of the world's leading scientific experts, who along with PureTech's team of biopharma pioneers, entrepreneurs and seasoned Board, identify, invent, and clinically de-risk new medicines. With this experienced team pursuing cutting edge science, PureTech Health is building the biopharma company of the future focused on improving and extending the lives of people with serious disease. For more information, visit www.puretechhealth.com or connect with us on Twitter [@puretechh](#).

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 regulatory filings for PureTech Health plc. 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 and regulatory requirements, 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.

This announcement contains inside information for the purposes of Article 7 of Regulation (EU) 596/2014.