



PureTech's Karuna Announces Initiation of Phase 2 Study with Proprietary Lead Product Candidate KarXT for the Treatment of Schizophrenia

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Phase 2 study aims to reproduce significant efficacy previously observed in schizophrenia trial with xanomeline alone

Company also announces successful Phase 1 study of proprietary xanomeline and trospium chloride formulation, which will be used in Phase 2 study

PureTech Health plc (LSE: PRTC) ("PureTech Health"), an advanced biopharmaceutical company developing novel medicines for dysfunctions of the Brain-Immune-Gut (BIG) Axis, is pleased to note that Karuna Pharmaceuticals, Inc ("Karuna"), an affiliate of PureTech Health, today announced the initiation of a Phase 2 study of KarXT (Karuna-Xanomeline-Trospium), its lead product candidate, for the treatment of psychosis in schizophrenia.

In a second Phase 1 study completed by Karuna, a proprietary co-formulation of KarXT successfully demonstrated tolerability at a dose level exceeding those shown to be efficacious in previous studies of xanomeline alone. Results from this Phase 1 study supported dose selection for the Phase 2 study, which is aimed at reproducing significant efficacy previously observed in a schizophrenia trial with xanomeline alone. Top-line data results are expected at the end of 2019.

Eric Elenko, PhD, Chief of Research and Strategy at PureTech Health, said: "We are pleased with the progress Karuna has made to advance KarXT into a Phase 2 study, bringing us one step closer to potentially delivering the first new mechanism in more than 60 years for the treatment of psychosis in schizophrenia. We have now demonstrated the tolerability of KarXT in two Phase 1 studies, including most recently with a proprietary formulation of KarXT, and we look forward to the results from the Phase 2 study."

The full text announcement from Karuna is as follows:

Karuna Announces First Patient Dosed in Phase 2 Study of Lead Product Candidate KarXT for the Treatment of Schizophrenia

Phase 2 study aims to reproduce significant efficacy previously observed in schizophrenia trial with xanomeline alone

Company also announces successful Phase 1 study of proprietary xanomeline and trospium chloride co-formulation, which will be used in Phase 2 study

BOSTON, October 15, 2018—[Karuna Pharmaceuticals, Inc.](#) ("Karuna"), focused on targeting muscarinic cholinergic receptors for the treatment of neuropsychiatric disorders marked by psychosis and cognitive impairment, today announced the initiation of a Phase 2 study evaluating the efficacy and safety of its lead product candidate, KarXT (Karuna-Xanomeline-Trospium), for the treatment of psychosis in schizophrenia. The study will use a co-formulation of KarXT, which was well-tolerated at dose levels exceeding those shown to be efficacious in previous xanomeline studies. Top-line data results from the Phase 2 study are expected at the end of 2019.

"We are excited to progress our development of KarXT, which has the potential to be the first antipsychotic drug with a unique mechanism in over 60 years and one which could be effective in treating not only positive symptoms but also the disabling negative and cognitive symptoms of the disease. Our Phase 2 study uses the same fundamental design as the successful efficacy study conducted previously with xanomeline alone," said Steve Paul, MD, Chief Executive Officer of Karuna. "We have designed KarXT as a novel approach to reduce the cholinergic side effects related to the activation of peripheral muscarinic receptors that were observed in previous studies by Eli Lilly. We have now demonstrated the improved tolerability in two Phase 1 studies, including with the proprietary co-formulation of xanomeline and trospium."

Karuna's KarXT was evaluated in a Phase 1 dose-ranging study that enrolled 70 healthy volunteers and successfully demonstrated tolerability at dose levels exceeding those shown to be efficacious in previous studies of xanomeline alone. The co-formulation also achieved exposure levels equivalent to or higher than the separate dosage forms used previously, and the results supported dose selection to be carried forward into Phase 2. There were no severe or serious adverse events reported in the co-formulation study. Side effects associated with KarXT were mild-to-moderate and transient in nature, often only lasting a few hours, and they were consistent with the previous KarXT study that used separate dosage forms for xanomeline and trospium.

The Phase 2 study is a double-blind, placebo-controlled study designed to evaluate the efficacy and safety of KarXT in approximately 160 patients with schizophrenia. The primary endpoint is total change from baseline Positive and Negative Syndrome Scale (PANSS) score compared to placebo. Additional endpoints will assess cognitive and negative symptoms in addition to general symptomology. The study employs a flexible dose design where patients are randomised in a 1:1 ratio to receive either KarXT or placebo for 5 weeks. Patients assigned to the KarXT arm will be treated with 100/20 mg xanomeline/trospium with the option to increase the dose to 125 mg/30mg xanomeline/trospium after the first week of the study.

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 only 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 KarXT

[KarXT](#) (Karuna-Xanomeline-Trospium) is Karuna's lead investigational product candidate for the treatment of psychosis in schizophrenia. It 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 central nervous system (CNS). KarXT is designed to selectively target M1/M4 muscarinic receptors in the brain while blocking their activation in peripheral tissues to significantly improve tolerability. Results from a Phase 1 study demonstrating the improved tolerability of KarXT vs xanomeline alone were announced in 2016, and a more recent Phase 1 study completed in 2018 supported the development of a co-formulation of KarXT that is now being evaluated in a Phase 2 study.

About Karuna Pharmaceuticals

Karuna is a clinical-stage drug development company targeting muscarinic cholinergic receptors for the treatment of psychosis and cognitive impairment across central nervous system (CNS) disorders, including schizophrenia and Alzheimer's disease, as well as pain. Karuna's lead product candidate, [KarXT](#) (Karuna-Xanomeline-Trospium), is being evaluated in a Phase 2 study in people with schizophrenia, with top-line results anticipated at the end of 2019. Karuna, which was founded by [PureTech Health](#) (LSE: PRTC), has a worldwide exclusive license for xanomeline and has an intellectual property portfolio more broadly covering selective muscarinic targeting enabled by the KarXT approach. For more information, visit www.karunapharma.com.

About PureTech Health

PureTech Health (LSE: PRTC) is an advanced biopharmaceutical company developing novel medicines for dysfunctions of the Brain-Immune-Gut (BIG) Axis. The Company has developed deep insights into the connection between the individual components of these systems and the resulting role in many chronic diseases, which have proven resistant to established therapeutic approaches. By harnessing this emerging field of human biology, PureTech Health is developing new categories of medicines with the potential to have great impact on people with serious diseases.

PureTech Health is advancing a rich pipeline of innovative therapies across two divisions: the Affiliates division and the Internal division. Its Affiliates division includes two product candidates that have been filed with the US Food and Drug Administration (FDA) for review and several other novel clinical and pre-clinical programmes. These affiliates are developing ground-breaking platforms and therapeutic candidates in collaboration with some of the world's leading experts.

PureTech's Internal division is advancing a pipeline fuelled by recent discoveries in lymphatics and immune cell trafficking to modulate disease in a tissue-specific manner. These programmes leverage the transport and biodistribution of various immune system components for the targeted treatment of diseases with major unmet needs, including cancers, autoimmune diseases, and neuroimmune disorders.

For more information, visit www.puretechhealth.com or connect with us on Twitter [@puretechh](https://twitter.com/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.