Karuna Doses First Subject in Tolerability Proof-of-Concept Study of Lead Product Candidate

BOSTON, Massachusetts, September 12, 2016 -- Karuna Pharmaceuticals, a company focused on targeting muscarinic receptors for the treatment of central nervous system (CNS) disorders including schizophrenia and Alzheimer's disease, today announced the dosing of the first subject in a tolerability proof-of-concept study of its proprietary lead product KarXT (xanomeline plus trospium chloride). The study, which will be conducted in up to 70 healthy individuals, aims to evaluate the tolerability of KarXT compared to xanomeline alone.

Exclusively licensed to Karuna, xanomeline is a novel, muscarinic acetylcholine receptor agonist that has demonstrated robust efficacy in treating schizophrenia and psychosis in Alzheimer's disease; however, it has also been associated with tolerability issues that have hindered its development. In a double-blind, placebo-controlled, monotherapy study in people with schizophrenia, a statistically significant, 24-point reduction over placebo was observed on the Positive and Negative Syndrome Scale (PANSS), a standard tool used to measure symptom severity in people with schizophrenia. By selectively targeting muscarinic receptors in the CNS with the KarXT approach, Karuna aims to reduce the peripheral cholinergic side effects previously seen with xanomeline alone.

"In clinical studies, xanomeline has shown robust efficacy in people with schizophrenia and in people with Alzheimer's disease, demonstrating the immense potential of targeting the M1/M4 muscarinic acetylcholine receptors; however, the muscarinic field has been stymied by tolerability concerns caused by activation of muscarinic receptors in peripheral tissues," said Andrew Miller, Ph.D., Karuna's Chief Executive Officer. "By combining xanomeline with trospium chloride, we aim to unlock the therapeutic potential of M1/M4 agonists and address the significant unmet need in treating these disorders."

The randomized, double-blind, multiple-dose study will dose up to 70 healthy volunteers aged 18 to 60 for in-clinic treatment over the course of nine days. Following a two-day run-in period with trospium alone, subjects will receive xanomeline with either trospium chloride or placebo. Top-line results are expected by the end of 2016.

About Karuna

Karuna is a clinical-stage drug development company targeting muscarinic receptors for the treatment of central nervous system (CNS) disorders. Karuna's lead program, KarXT, is a product candidate consisting of **x**anomeline, a novel muscarinic acetylcholine receptor agonist that has demonstrated efficacy in placebo-controlled human trials in schizophrenia and Alzheimer's disease, and **t**rospium chloride, an FDA-approved and well-established muscarinic receptor antagonist that has been shown not to enter the CNS.

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, and it typically includes psychotic episodes. Antipsychotics are the mainstay therapy for the treatment of schizophrenia; however, significant unmet needs remain due to the limited efficacy and potential serious side effects associated with current antipsychotic medications.

Alzheimer's disease is a chronic, progressive, neurodegenerative disorder characterized by loss of memory and other important mental functions. The type, severity, sequence and progression of mental changes vary widely, and it represents an enormous burden on victims of the disease and their families. Alzheimer's is the most common form of dementia in people over the age of 65, and it is

estimated to affect more than 5 million Americans. It is the sixth leading cause of death in the United States, and there is currently no cure.

Karuna's Board of Directors includes Ben Shapiro, M.D., former Executive Vice President of Research for Merck & PureTech Health Non-Executive Director; Edmund Harrigan, M.D., former Senior Vice President for Worldwide Safety and Regulatory, Head of Worldwide Business Development at Pfizer; and Atul Pande, M.D., Former Senior Vice President, Head of Neuroscience and Senior Advisor, Pharmaceutical R&D at GlaxoSmithKline & PureTech Health Senior Advisor. Karuna's Chief Clinical Advisor is Alan Breier, M.D., the former Chief Medical Officer at Eli Lilly. Karuna 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.

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.

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