Preclinical Characterization of Novel B2-Receptor Antagonists Published in *Frontiers in Pharmacology*

Data further validate Pharvaris' B2-receptor-antagonist program

Zug, Switzerland, July 30, 2020 – Pharvaris, a clinical-stage company focused on the discovery and development of novel oral B2-receptor antagonists for the treatment of hereditary angioedema (HAE) and other B2R-receptor-mediated indications, has published data describing a novel class of small molecule bradykinin (BK) B2-receptor antagonists. Preclinical data appear in a recent open-access article in *Frontiers in Pharmacology* demonstrating potency, mechanism, and properties consistent with oral bioavailability.

"This novel chemical class provided a significant stepping-stone for the discovery of PHA121, a highly-selective, potent, and orally bioavailable B2-receptor antagonist," said Anne Lesage, Ph.D., Chief Early Development Officer of Pharvaris and lead author on the publication. "PHA121 is the only oral B2-receptor antagonist in clinical development, currently in Phase 1 for the treatment of HAE. The substantial experience in and deep understanding of HAE within the Pharvaris team enabled the discovery of this class of molecules and supports our mission to significantly impact the treatment paradigm for B2-receptor-mediated diseases."

The data set found in the publication demonstrates the preclinical profile of the new class of molecules relative to icatibant, an injectable B2-receptor antagonist used as the leading therapy for on-demand treatment of HAE. For example, one novel B2-receptor antagonist described in this paper was found to be 40-fold more potent than icatibant in antagonizing human B2 (respectively, IC_{50} 210 pM versus 8.7 nM); to show substantially higher metabolic stability; and, is predicted to show high oral absorption. Further characterization of this particular molecule showed that the molecule selectively antagonized the B2-receptor relative to a panel with more than one hundred different molecular targets including G protein-coupled receptors, such as the bradykinin B1 receptor.

The full publication can be found here: https://doi.org/10.3389/fphar.2020.00916

About PHA121

PHA121 (PHA-022121) is a highly potent, specific, and orally bioavailable competitive antagonist of the bradykinin B2 receptor and is currently in Phase 1 clinical development for the treatment of HAE. PHA121 utilizes the same mechanism as icatibant, the leading therapy for on-demand treatment of HAE. Pharvaris is developing this novel small molecule for on-demand and prophylactic treatment of HAE and other bradykinin-mediated disease. Emerging clinical data from the ongoing Phase 1 study in healthy volunteers confirm PHA121's oral bioavailability and rapid exposure and demonstrate that PHA121 has been observed to be safe and well-tolerated at the doses studied to date.

About Pharvaris

Pharvaris is a clinical-stage company focused on bringing oral B2-receptor antagonists to patients. By targeting this clinically proven therapeutic target with novel small molecules, the Pharvaris team is advancing new alternatives to injected therapies for all sub-types of HAE and other B2-receptor-mediated diseases. The company brings together executives with a breadth of expertise across pharmaceutical development and rare disorders, including HAE. For more information, visit https://pharvaris.com/.

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