Annovis Bio Announces Publication of ANVS401 Mechanism of Action in Peer-Reviewed Pharmaceutics

ANVS401 (Posiphen) Inhibits the Translation of mRNAs of Neurotoxic Proteins Responsible for the Progression of Neurodegenerative Diseases

Berwyn, Pennsylvania--(Newsfile Corp. - December 14, 2021) - Annovis Bio, Inc. (https://www.newsfilecorp.com/redirect/oJ2nMcrVyO) (NYSE: ANVS) ("Annovis" or the "Company"), a clinical-stage drug platform company addressing Alzheimer's disease (AD), Parkinson's disease (PD), and other neurodegenerative diseases, today announced the publication of ANVS401's mode of action in the peer-reviewed journal *Pharmaceutics* with the manuscript titled "Posiphen Reduces the Levels of Huntingtin Protein through Translation Suppression (https://www.newsfilecorp.com/redirect/OLwZ0HmyWQ)".

ANVS401 (Posiphen) is an oral molecule that was shown to inhibit APP and α-Syn protein translation in previous studies. To understand how it inhibits translation, two complementary approaches were undertaken: a macro approach to examine all proteins in the cell whose translation is affected by ANVS401 and a micro approach to study the mechanism of action using molecular biology to understand and validate the binding and function.

First, the non-biased proteomics approach was applied to explore what proteins in the total protein universe were specifically downregulated by ANVS401. The results demonstrated that, in addition to the proteins already known to be reduced by ANVS401, other neurotoxic aggregating proteins - huntingtin protein (HTT) and TDP43 - were shown to be downregulated as well.

A detailed analysis of the reduction of these protein levels was conducted in five different laboratories using multiple methodologies. It revealed that the mRNAs of these proteins have a special region, an atypical stem loop, that is preserved and responsible for their translation. When this region is bound to an RNA binding protein, the mRNA is not translated. When this region is free, the mRNA is translated. In neurodegenerative conditions, the mRNA coding for these neurotoxic proteins is over-translated and produces high levels of these proteins and their onset of toxicity. ANVS401 specifically increases the affinity between this special region and the RNA binding protein, thereby preventing the mRNA from being released and translated. This leads to lower translation, lower levels of neurotoxic proteins, and less toxicity in the brain.

"These results support and cement the previous data about ANVS401's ability to reduce the translation of several neurotoxic proteins. Our rigorous approach to understanding the mode of action shows that while ANVS401 does lower the levels of more than one neurotoxic protein, it is exquisitely specific for the atypical stem loops in the mRNAs of these proteins," commented Founder, President, and CEO of Annovis, Maria L. Maccecchini, Ph.D.

About Annovis Bio, Inc.

Headquartered in Berwyn, Pennsylvania, Annovis Bio, Inc. (Annovis) is a clinical-stage, drug platform company addressing neurodegeneration, such as Alzheimer's disease (AD), Parkinson's disease (PD), and Alzheimer's in Down Syndrome (AD-DS). We believe that we are the only company developing a drug for AD, PD, and AD-DS that inhibits more than one neurotoxic protein and, thereby, improves the information highway of the nerve cell, known as axonal transport. When this information flow is impaired, the nerve cell gets sick and dies. We conducted two Phase 2 studies: one in AD patients and one in both AD and PD patients. In the AD/ PD study our drug improves memory loss and dementia associated with AD, as well as body and brain function in PD.

For more information on Annovis Bio, please visit the company's website www.annovisbio.com (https://www.newsfilecorp.com/redirect/PMo1RHx1Pw) and follow us on LinkedIn (https://www.newsfilecorp.com/redirect/w2znDFwmY4), and Twitter (https://www.newsfilecorp.com/redirect/gxKAMHGgQk).

Forward-Looking Statements

Statements in this press release contain "forward-looking statements" that are subject to substantial risks and uncertainties. Forward-looking statements contained in this press release may be identified by the use of words such as "anticipate," "expect," "believe," "will," "may," "should," "estimate," "project," "outlook," "forecast" or other similar words, and include, without limitation, statements regarding the timing, effectiveness, and anticipated results of ANVS401 clinical trials. Forward-looking statements are based on Annovis Bio, Inc.'s current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Further, certain forward-looking statements are based on assumptions as to future events that may not prove to be accurate. These and other risks and uncertainties are described more fully in the section titled "Risk Factors" in the Annual Report on Form 10-K for the year ended December 31, 2020, filed with the Securities and Exchange Commission. Forward-looking statements contained in this announcement are made as of this date, and Annovis Bio, Inc. undertakes no duty to update such information except as required under applicable law.

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