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Alpha Cognition Announces Positive Data from Pre-Clinical Studies of ALPHA-0602 (Progranulin) for Amyotrophic Lateral Sclerosis (ALS)

VANCOUVER, B.C., March 29, 2022. **Alpha Cognition Inc. (TSX-V: ACOG) (OTCQB: ACOGF)** ("Alpha Cognition" (ACI), or the "Company"), a biopharmaceutical company committed to developing novel therapies with the potential to transform the lives of people with debilitating neurodegenerative disorders, is pleased to announce positive preclinical data from their ALPHA-0602 ALS gene therapy program. These data underscore the robust preclinical evidence supporting Alpha Cognition's AAV-based gene therapy approach to treating ALS and highlight the Company's strategy to validate these data in planned clinical trials.

Denis Kay, the Company's Chief Scientific Officer commented: "ALS is a devastating disease with patients in urgent need of effective therapies. Alpha-0602 is designed to increase brain progranulin (PGRN) levels and provide support for the motor system through the reduction of TDP-43 and FUS pathology, as well as reducing neuroinflammation and the effects of oxidative stress, associated with ALS. These benefits have been observed in preclinical studies and strongly support the continued development of ALPHA-0602 for the treatment of ALS."

Highlights of the positive proof of concept pre-clinical results demonstrated with ALPHA-0602 *in vitro* in motor neurons and *in vivo* in models of ALS, include:

- ALPHA-0602 demonstrated abundant PGRN expression in motor neurons, suggesting a neurotrophic role for PGRN. ALPHA-0602 further increased PGRN levels and decreased motor neuron cell death in *in vitro* models.
- Using an *in vivo* model of ALS to further assess the neurotrophic effects of PGRN, ALPHA-0602 reversed the motor neuron toxicity resulting from both decreased levels of TDP-43 and FUS, and expression of ALS related toxic forms of these proteins.
- In an ALS transgenic mouse model caused by a toxic form of TDP-43, Alpha-0602 administered via adeno-associated virus, resulted in successful viral transduction of CNS cells and substantially increased cerebrospinal fluid (CSF) levels of PGRN.
- ALPHA-0602 treated TDP-43 transgenic mice persistently gained weight throughout the 10-week study, in contrast to untreated transgenic animals who failed to gain weight. Continued weight gain in the face of a significant and sustained toxic insult, is indicative of a therapeutic benefit of Alpha-0602 expression.

"Collectively, these new insights from our preclinical research further support the development of ALPHA-0602 for the treatment of the motor neuron degeneration associated with ALS," said Michael McFadden, Alpha Cognition's Chief Executive Officer. "This represents an important milestone for our company, and we plan to assess the effect of progranulin expression on the neuropathology associated with this animal model as a next step in our development program."

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About Alpha Cognition Inc.

Alpha Cognition Inc. is a clinical stage, biopharmaceutical company dedicated to developing treatments for patients suffering from neurodegenerative diseases, such as Alzheimer's disease and Amyotrophic Lateral Sclerosis (ALS), for which there are limited treatment options.

ALPHA-1062, is a patented new chemical entity being developed as a new generation acetylcholinesterase inhibitor for the treatment of Alzheimer's disease, with expected minimal gastrointestinal side effects. ALPHA-1062's active metabolites is differentiated from donepezil and rivastigmine in that it binds neuronal nicotinic receptors, most notably the alpha-7 subtype, which is known to have a positive effect on cognition. ALPHA-1062 is also being developed in combination with memantine to treat moderate to severe Alzheimer's dementia and as an intranasal formulation for traumatic brain injury.

ALPHA-0602 (Progranulin) is expressed in several cell types in the central nervous system and in peripheral tissues, it promotes cell survival, regulates certain inflammatory processes, and plays a significant role in regulating lysosomal function and microglial responses to disease. Its intended use for the treatment of neurodegenerative diseases has been patented by the Company and Alpha-0602 has been granted an Orphan Drug Designation for the treatment of ALS by the FDA.

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This news release includes forward-looking statements within the meaning of applicable securities laws. Except for statements of historical fact, any information contained in this news release may be a forward-looking statement that reflects the Company's current views about future events and are subject to known and unknown risks, uncertainties, assumptions and other factors that may cause the actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Forward-looking statements can be identified by the words "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective,"

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This news release may also contain estimates and other statistical, market and industry data from independent parties or made by the Company relating to our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. We cannot guarantee the accuracy and completeness of information from third party sources.