Aardvark Therapeutics Announces FDA Orphan Drug Designation Granted to ARD-101, a Novel Drug Candidate for Prader-Willi Syndrome

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- The FDA granted Aardvark Orphan Drug Designation for the use of ARD-101 in Prader-Willi Syndrome (PWS), a rare genetic disease characterized by extreme and unabating hunger.
- FDA decision is based on early results of an ongoing Phase 2 trial of oral ARD-101 in young adults with PWS

SAN DIEGO, June 20, 2023 /PRNewswire/ -- Aardvark Therapeutics, Inc., a clinical stage biopharmaceutical company, today reported receipt of an Orphan Drug Designation from the FDA for its lead program, ARD-101, an oral small molecule bitter taste receptor (TAS2R) agonist. The early clinical study results suggest a promising future for a new class of pharmaceuticals that could benefit people with insatiable hunger (hyperphagia) and aggressive food-seeking behaviors, as well as for obesity and metabolic conditions, which are prominent features of the rare genetic condition PWS. Thus far, no drug has been approved by the FDA to treat the hyperphagia associated with PWS.

Prader-Willi Syndrome (PWS)

PWS is a severe neurodevelopmental disorder with a prevalence of about 1 in 15,000-20,000 births. The disorder is caused by the loss of function of several genes located on chromosome 15. PWS impacts multiple organ systems and is characterized by metabolic, endocrine, and neurological dysfunction. One of the hallmark characteristics of PWS is morbid obesity in early childhood, accompanied by developmental delays and musculoskeletal malformations. Obesity in PWS is driven by hyperphagia and mitigated by strict control of food intake. The strict food control, if anything, exacerbates the hyperphagia and is stressful for those afflicted as well as the caregivers.

ARD-101 is differentiated from other treatment options.

ARD-101 has been shown to be safe and substantially gut-restricted. Yet ARD-101 conveys its systemic effects by activating secretion of several gut peptide hormones, including GLP-1, GLP-2, and cholecystokinin (CCK). Gut CCK has long been recognized as the "satiety signal", acting via the gut-brain axis, to control hunger. While PWS patients have a normal CCK receptor, their CCK release from gut enteroendocrine I-cells in response to food is impaired, leaving PWS patients with a continuous sense of extreme hunger.

"Aardvark has discovered a way to stimulate the release of naturally produced gut CCK. Early trial results show substantial inhibition of hunger symptoms, *i.e.* hyperphagia" said Tien Lee, MD, CEO of Aardvark. "Our team is working towards initiating pivotal studies with ARD-101 for the treatment of PWS. We appreciate the close collaboration with the study principal investigators, Dr. Diane Stafford at Stanford Children's Health, and Dr. Shawn McCandless at Colorado Children's Hospital. We further appreciate invaluable support we have received from the Foundation for Prader-Willi Research, the PWS Association USA, and the International PWS Organization, to help us explore this novel treatment approach as a potential option for patients suffering from PWS."

Dr. McCandless, Chair, Department of Genetics and Metabolism, Children's Hospital Colorado said: "We are pleased to see several individuals with PWS benefit from the short-term exposure to ARD-101, experiencing substantial decreases in hunger and food-seeking behavior and improved quality of life for them and their families while using the product. With the confirmed safety and tolerability as well as the early efficacy signal, we are now excited to further explore the therapeutic potential of this novel drug in people with PWS."

Dr. Stafford, Clinical Professor Pediatrics, Endocrinology and Diabetes at Stanford University added: "We are truly encouraged by the early findings of our ongoing trial of oral ARD-101 in young adults with PWS. We look forward to rapidly expanding the clinical evaluation of this well-tolerated oral drug and hope to bring a safe and effective treatment to patients in need".

The Foundation for Prader-Willi Research (FPWR) has supported the ARD-101 clinical research program from its inception. FPWR's Director of Research Programs, Dr. Theresa Strong, said:

"there is an urgent need for safe and effective treatments for individuals with PWS. We are so pleased to see the FDA grant Orphan Drug Designation to ARD-101 in recognition of its therapeutic potential based on the promising early clinical findings".

About ARD-101

Aardvark's lead product, ARD-101, is a first-in-class oral composition that has shown promising activity in reducing hunger and promoting weight loss in pre-clinical studies. Phase I studies demonstrated safety and tolerability in healthy human volunteers; three Phase II studies have demonstrated an impact on hunger suppression with associated metabolic benefits. ARD-101 is

substantially gut-restricted with minimal systemic exposure yet conveys systemic effects via activation of gut peptide hormone secretion, including the satiety signal CCK.

About Aardvark Therapeutics, Inc.

Aardvark Therapeutics is a clinical stage biopharmaceutical company focused on developing novel small molecule therapeutics to activate innate homeostatic pathways for the treatment of metabolic diseases, inflammation, and other indications. Founded in 2017, the company has now advanced ARD-101 to Phase II clinical trials. Aardvark has multiple other programs in its pipeline.

For more information visit www.aardvarktherapeutics.com.

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