



Aardvark Therapeutics Presents Data Supporting its Metabolic Obesity Pipeline Programs at ObesityWeek 2025

November 4, 2025

New preclinical results demonstrate the potential of ARD-201 in enhanced glucose control, along with preservation of lean mass, underscoring its opportunity in addressing key challenges in today's obesity treatment landscape

Preclinical and clinical data demonstrates the potential of ARD-201 to attenuate weight gain, promote weight loss and help maintain weight after the discontinuation of GLP-1RA

Aardvark to host investor webinar on November 5th, 2025 to review ARD-101 and ARD-201 programs, as well as ObesityWeek presentations

SAN DIEGO, Nov. 04, 2025 (GLOBE NEWSWIRE) -- Aardvark Therapeutics, Inc. (Aardvark) (Nasdaq: AARD), a clinical-stage biopharmaceutical company focused on developing novel, small-molecule therapeutics to activate innate homeostatic pathways for the treatment of metabolic diseases, presented data today at the ObesityWeek 2025 conference demonstrating the mechanistic rationale and therapeutic potential of two of its metabolic obesity programs, including ARD-201.

"More than 50% of patients stop taking GLP-1 therapies within 3 months, often resulting in rapid weight regain," said Tien Lee, M.D., Founder and Chief Executive Officer of Aardvark. "ARD-201 combines the noted anti-hunger and metabolic effects of ARD-101 with the synergistic properties of sitagliptin to enhance the anti-appetite effects of ARD-101 to create a potential first-in-class therapy that may overcome the tolerability and rebound challenges of GLP-1 therapies. We're looking forward to advancing ARD-201 into two Phase 2 trials, POWER and STRENGTH, to further evaluate its potential for individuals living with metabolic obesity."

ARD-201 Obesity Program

ARD-201 is planned to be a fixed-dose combination of the TAS2R agonist ARD-101 and the DPP-4 inhibitor sitagliptin. The co-administration of these two compounds will be tested in the Phase 2 POWER Trial (**P**revention **O**f **WE**ight **R**egain) expected to commence by the end of 2025.

Poster Title: TAS2R Agonist ARD-101 Attenuates Weight Gain in Mice and Reduces Hunger in Adults with Obesity

Summary: Preclinical and clinical data support the continued development of ARD-201 to attenuate weight gain, promote weight loss, and help maintain weight after the discontinuation of glucagon-like peptide-1 receptor agonist (GLP-1RA) therapies. In addition, ARD-201 improved glucose tolerance and lean body mass composition.

Notable findings:

- **Preclinical – ARD-201 (Validated Diet-Induced Obesity (DIO) Mouse Model):**
 - ARD-201 reduced fat mass comparable to high-dose tirzepatide but, unlike tirzepatide, preserved lean mass
 - ARD-201 alone achieved glucose control comparable to high-dose tirzepatide, and in combination with low-dose tirzepatide delivered the most rapid glucose clearance
 - Previously reported preclinical data demonstrated ARD-201 reduced body weight by ~19% after 30 days, which was comparable to high-dose tirzepatide
 - Previously reported preclinical data demonstrated ARD-201 ~30% weight loss when combined low-dose tirzepatide
- **Clinical – ARD-101 (Randomized, Placebo-Controlled, Phase 2A Study in Adults with Obesity):**
 - ARD-101 showed signals of weight control, reduced hunger, and improved metabolic parameters, particularly among participants with elevated baseline values
 - ARD-101 was well tolerated, with no serious adverse events or treatment discontinuations, reflecting a distinct profile from the effects associated with current anti-obesity therapies

WE-868 Obesity Program

WE-868 is a small molecule isoflavonoid designed to modulate oxidative phosphorylation and represents a potentially novel pathway for promoting weight loss and additional metabolic benefits.

Poster Title: An Isoflavonoid Modulator of Oxidative Metabolism with Therapeutic Potential in Obesity and Diabetes

Summary: A clinical study of WE-868 showed a correlation between treatment and weight loss in patients in another indication, and subsequent preclinical studies explored the mechanism as a novel treatment for obesity. An additional preclinical study showed that WE-868 shifts cellular energy metabolism by modulating oxidative phosphorylation.

Notable findings:

- In preclinical studies, WE-868 dose-dependently prevented high-fat diet (HFD)-induced weight gain, with the higher dose inducing net weight loss
- In DIO mice, significant weight loss was seen in medium and high dose WE-868 compared to semaglutide

Aardvark to Host an Investor Webinar on November 5

Aardvark will host an investor webinar on Wednesday, November 5th, 2025 from 5:00 p.m. to 7:00 p.m. ET to provide an overview of ARD-101, ARD-201 and WE-868 data presented at ObesityWeek. The event will feature a discussion with leading key opinion leaders Tony Lam, Ph.D., Professor at the University of Toronto, and Caroline Apovian, M.D., Co-Director at Center for Weight Management and Wellness at Brigham and Women's Hospital. The event will also feature a discussion on ARD-101 in Prader-Willi Syndrome with Stacy Ward, MS, BCBA, Chief Executive Officer of Prader-Willi Syndrome Association - USA, and Dorothea Lantz, Director of Community Engagement at Prader-Willi Syndrome Association - USA.

The live webcast presentation will be accessible on the company's website, <https://ir.aardvarktherapeutics.com/news-events/events>, under the investors section, and an archived recording will be available on the website following the presentation.

About ARD-101

ARD-101 is a gut-restricted small molecule agonist of select taste receptors (TAS2Rs) expressed on the luminal side of the intestine. As a potent bitter taste receptor pan-agonist, ARD-101 stimulates enteroendocrine cells of the digestive tract to release multiple gut-peptide hormones including GLP-1 and the satiety hormone cholecystokinin (CCK), which activates gut-brain neurologic signaling to mediate hunger. ARD-101 has demonstrated an ability to reduce hunger when used alone or in combination with currently available GLP-1 therapies. The FDA has granted ARD-101 both Orphan Drug Designation and Rare Pediatric Disease Designation for PWS.

ARD-101 is being evaluated in the Phase 3 HERO trial for hyperphagia associated with PWS.

About ARD-201

ARD-201 is planned to be an oral fixed-dose combination of a dipeptidyl peptidase-4 (DPP-4) inhibitor and the TAS2R agonist ARD-101. These receptors normally respond to nutrients and are part of the gut-brain axis that helps regulate food intake. Activation of TAS2Rs stimulates the release of endogenous signaling molecules, including CCK and GLP-1, which play key roles in promoting satiety and reducing hunger. DPP-4 inhibitors, which are widely used for the treatment of diabetes, extend the biological activity of gut hormones, including GLP-1, by preventing their enzymatic inactivation. Together, these mechanisms allow ARD-201 to enhance and prolong the body's natural signals for fullness.

Aardvark is advancing ARD-201 in two Phase 2 trials:

- Expected to initiate in the second half of 2025, ARD-201 will be evaluated in the Phase 2 POWER trial for the potential to prevent weight regain in subjects who discontinue GLP-1RA therapy after achieving substantial prior weight loss (~15%).
- Planned for initiation in the first half of 2026, ARD-201 will be evaluated in the Phase 2 STRENGTH trial for potential placebo-adjusted weight loss and the additive effects of ARD-201 combined with GLP-1RA therapy.

About WE-868

WE-868 is a novel, small molecule that modulates mitochondrial energy metabolism without directly suppressing the OXPHOS pathway. It is being evaluated in preclinical studies for the potential treatment of obesity and diabetes.

About Aardvark Therapeutics, Inc.

Aardvark is a clinical-stage biopharmaceutical company developing novel, small-molecule therapeutics designed to suppress hunger for the treatment of Prader-Willi Syndrome and metabolic diseases. Recognizing hunger (the discomfort from not having eaten recently) is a distinct neural signaling pathway separate from appetite (the reward-seeking, desirability of food). Our programs explore therapeutic applications in hunger-associated indications and potential complementary uses with anti-appetite therapies. Our lead compound, oral ARD-101, is in Phase 3 clinical development for the treatment of hyperphagia associated with PWS, a rare disease characterized by insatiable hunger. Aardvark is also developing ARD-201, a planned fixed-dose combination of ARD-101 with a DPP-4 inhibitor, and conducting two separate trials with a goal of addressing some of the limitations of currently marketed GLP-1 therapies for the treatment of obesity and obesity-related conditions. For more information, visit aardvarktherapeutics.com.

Forward-Looking Statements

Statements in this press release about future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute "forward-looking statements." These statements include, but are not limited to, statements concerning: Aardvark's business strategy; product candidates and programs, including ARD-201, ARD-101 and WE-868; ongoing clinical trials; planned clinical trials; expected timing for data readouts and reporting topline results; likelihood of success; as well as plans and objectives for future operations; ARD-201's potential, including its potential as a first-in-class therapy and ability to overcome the tolerability and rebound challenges of GLP-1 therapies; and Aardvark's upcoming webinar and the topics expected to be discussed in such webinar. The words, without limitation, "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these or similar identifying

words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: uncertainties related to potential delays in the commencement, enrollment and completion of clinical trials; the risk that Aardvark may use its capital resources sooner than expected and that they may be insufficient to allow Aardvark to achieve its anticipated milestones; risks related to its dependence on third parties for manufacturing, shipping and production of drug product for use in clinical and preclinical trials; the risk of unfavorable clinical trial results; the risk that results from earlier clinical trials and preclinical studies may not necessarily be predictive of future results; and other risks and uncertainties, including the factors described under the “Risk Factors” section of Aardvark’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2025 that the Company filed with the Securities and Exchange Commission on August 13, 2025. When evaluating Aardvark’s business and prospects, careful consideration should be given to these risks and uncertainties. Any forward-looking statements contained in this press release are based on the current expectations of Aardvark’s management team and speak only as of the date hereof, and Aardvark specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise, unless required by law.

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