MetaVia Announces Positive Top-Line Data From the 4-Week Phase 1 MAD Trial of DA-1726, a Novel 3:1 Ratio GLP-1 Glucagon Dual Receptor Agonist to Treat Obesity, Showing Compelling Weight Loss and Safety Effects With Potential Best-In-Class Glucose Control (GLP-1R), Waist Reduction (GCGR), and Tolerability

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With No Titration, Demonstrated Compelling Maximum Weight Loss of 6.3% and Mean Weight Loss of 4.3% at Day 26 at 32 mg Dose (p=0.0005)

Demonstrated Strong Signal of GLP-1R Efficacy with Maximum Lowering of Fasted Glucose of -18 mg/dL and Mean Lowering of -5.3 mg/dL at Day 26 at 32 mg Dose

Maximum Waist Circumference Reduction of 3.9 Inches and Mean Reduction of 1.6 Inches Demonstrates Strong Signal of Glucagon Efficacy at Day 33 at 32 mg Dose

Additional Cohorts Being Added to Determine Maximum Tolerated Dose

Planned Phase 1 Part 3 to Include Wegovy® Early Drop-Out Patients to Explore Potential Superiority of DA-1726 on Safety and Tolerability, Along With Weight Loss and Other Secondary Endpoints

CAMBRIDGE, Mass., April 15, 2025 /PRNewswire/ -- **MetaVia Inc.** (Nasdaq: MTVA), a clinical-stage biotechnology company focused on transforming cardiometabolic diseases, today announced positive results from the 4-week multiple ascending dose (MAD) Part 2 of its Phase 1 clinical trial of DA-1726, a novel, dual oxyntomodulin (OXM) analog agonist that functions as a glucagon-like peptide-1 receptor (GLP1R) and glucagon receptor (GCGR), for the treatment of obesity.

In the 28-day, 36-subject MAD portion of the study, DA-1726 demonstrated excellent safety and tolerability, with positive clinical activity. The cohort receiving 32 mg of DA-1726 with no titration demonstrated a maximum reduction in body weight from baseline ranging up to -6.3%, and a mean body weight reduction of -4.3% at Day 26 (p=0.0005). Four out of six subjects on the 32 mg dose experienced mild gastrointestinal (GI) adverse events (AEs), most of which were resolved after 24 hours of occurrence. There were no treatment-related discontinuations or serious adverse events (SAEs).

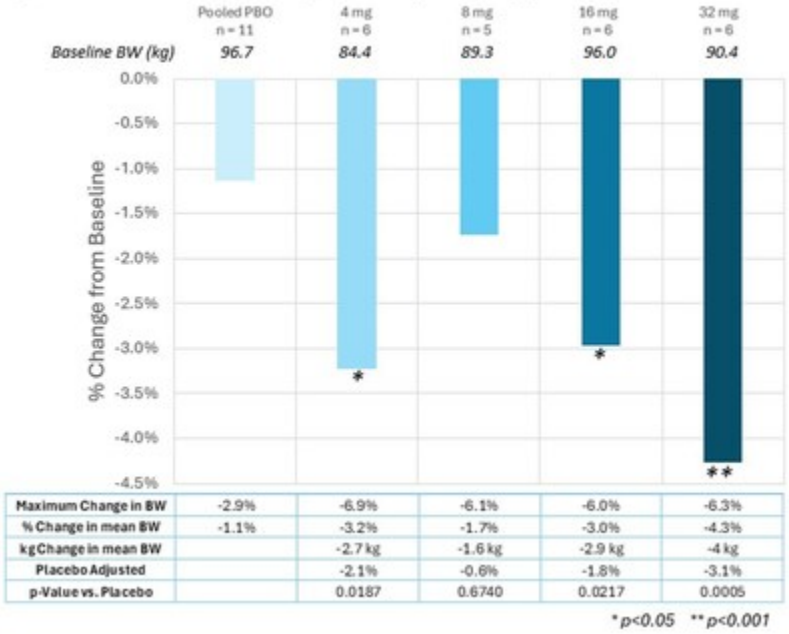
"The Phase 1 MAD data underscore DA-1726's potential as a best-in-class obesity drug demonstrating compelling safety, tolerability and strong weight loss effects," stated Hyung Heon Kim, President and Chief Executive Officer of MetaVia. "The data also indicates strong clinical characteristics, with compelling tolerability and a maximum weight loss of -6.3% at the 32 mg dose, which is not yet the maximum tolerated dose, along with a mean weight reduction of -4.3% from baseline. Although subjects in this study were exposed to study drug or placebo for a total of 26 days, no signs of plateau were observed. Given GLP-1R lowers glucose levels while GCGR increases them, the 3:1 ratio of DA-1726 may provide an optimal balance to achieve a sustainable and tolerable therapeutic effect in this class of drugs. Additionally, early satiety was observed in 83% (5 of 6) of patients on the 32 mg dose, which we believe may be suggestive of efficacy and we anticipate that greater weight loss may be seen in longer duration studies. With the mean baseline of 41 inches, DA-1726 showed a waist circumference reduction of 1.6 inches on average, with a maximum reduction of 3.9 inches by day 33, which we believe is a result of GCGR breaking down the white adipose tissue, as was reported in the preclinical poster we presented at EASL 2024. It is important to note that the mean waist circumference reductions were somewhat sustained with a 1.46 inch reduction almost a month after the last dosing. Further, DA-1726 demonstrated potentially best-in-class lowering of fasted glucose of -5.3 mg/dL and a maximum of -18 mg/dL at Day 26, allowing for a potential expansion into Type 2 Diabetes and obese MASH patients. Unlike amylin which reduces appetite, or GIP which controls AEs, glucagon has its own therapeutic target other than weight loss, mainly in the liver. DA-1726 shows strong signals that may benefit obese patients with at least one comorbidity, as per FDA guidance. Not all obese patients need to lose 30% of their weight and it is our goal to develop an obesity drug that can be used safely in all obese patients with different comorbidities.

"Despite DA-1726's glucagon agonism, fasting plasma glucose (FPG) was well controlled and showed reduction without any hypoglycemic AEs in all cohorts. The pharmacokinetic (PK) results demonstrated a favorable exposure profile and dose proportionality to support the proposed weekly dosing of DA-1726. Of note, no significant cardiovascular signals were observed in heart rate and QTcF results of the subjects receiving DA-1726. Additionally, only four subjects experienced mild GI-related AEs after the first 32 mg dose, most of which resolved within 24 hours, demonstrating a potentially significantly better tolerability profile compared to other weight loss treatments on the market."

Mr. Kim continued, "It is well known that many patients on current GLP-1 agonists discontinue treatment due to tolerability issues,

with 20% to 30% stopping within the first month and up to 70% within a year. With DA-1726's balanced activation of GLP1R and glucagon receptors enhancing energy expenditure, we remain confident in its potential to become a best-in-class obesity drug, with the further potential to offer superior tolerability than currently marketed GLP-1 agonists and those in late-stage clinical trials. Based on these results, we are currently planning to conduct a Phase 1 Part 3 study which will investigate DA-1726 on Wegovy® early drop-out patients. Our goal is to generate data showing the superiority of DA-1726 with respect to tolerability and safety, along with weight loss and other secondary endpoints. In parallel, based on the drug's clean safety profile, one or more additional cohorts with a higher dose will be added to the Phase 1 study in order to further explore the maximum tolerated dose, which will allow us to realize the full potential of DA-1726."

Figure 1. DA-1726 Mean Changes in Body Weight (%) at Day 26



Maximum Change in BW	-2.9%	-6.9%	-6.1%	-6.0%	-6.3%
% Change in mean BW	-1.1%	-3.2%	-1.7%	-3.0%	-4.3%
kg Change in mean BW		-2.7 kg	-1.6 kg	-2.9 kg	-4 kg
Placebo Adjusted		-2.1%	-0.6%	-1.8%	-3.1%
p-Value vs. Placebo		0.0187	0.6740	0.0217	0.0005

**p<0.05 **p<0.001*

DA-1726 demonstrated encouraging safety and tolerability following repeated dosing. Overall, 25% of subjects in the MAD study on DA-1726 experienced mostly mild (GI) related AEs, 12.5% of patients reported nausea (vs. 8.3% on placebo), 16.7% experienced vomiting (vs. 8.3% on placebo), 12.5% experienced constipation and 1 subject experienced abdominal distension. GI AEs were mostly transient in nature and resolved spontaneously within 1-3 days. Early satiety was observed in five out of six subjects receiving the 32 mg dose. Considering that most patients started experiencing this AE after the third dose, the company believes these findings suggest signs of efficacy and that greater weight loss may be seen in longer duration studies.

Table 1. Subject Disposition

Number of subjects (%)	Pooled PBO	4 mg	8 mg	16 mg	32 mg
Randomized	12	6	6	6	6
Completed the Study	10 (83.3 %)	6 (100 %)	5 (83.3 %)	6 (100 %)	6 (100 %)
Early Discontinuation from the Study	2 (16.7 %)	0	1 (16.7%)*	0	0
Reason for Study Discontinuation					
Treatment Related SAE	0	0	0	0	0
Non-Treatment Related SAE	0	0	1 (16.7%) *	0	0
Others	2 (16.7 %)	0	0	0	0

** Hospitalization due to a car accident, subject was in a passenger seat. Not related to IP.*

Table 2. GI Treatment Emergent Adverse Events, by Severity

GI Treatment Emergent Adverse Events Number of subjects reporting (%)	Pooled PBO n = 12	Pooled DA-1726 n = 24	4 mg n = 6	8 mg n = 6	16 mg n = 6	32 mg n = 6
Gastrointestinal disorders	1 (8.3 %)	6 (25.0 %)	1 (16.7 %)	0	1 (16.7 %)	4 (66.7 %)
Mild	1 (8.3 %)	5 (20.8 %)	1 (16.7 %)	0	0	4 (66.7 %)
Moderate	0	1 (4.2 %)	0	0	1 (16.7 %)	0
Severe	0	0	0	0	0	0
Vomiting	1 (8.3 %)	4 (16.7 %)	0	0	1 (16.7 %)	3 (50.0 %)
Mild	1 (8.3 %)	3 (12.5 %)	0	0	0	3 (50.0 %)

Moderate	0	1 (4.2 %)	0	0	1 (16.7 %)	0
Severe	0	0	0	0	0	0
Nausea	1 (8.3 %)	3 (12.5 %)	0	0	1 (16.7 %)	2 (33.3 %)
Mild	1 (8.3 %)	2 (8.3 %)	0	0	0	2 (33.3 %)
Moderate	0	1 (4.2 %)	0	0	1 (16.7 %)	0
Severe	0	0	0	0	0	0
Constipation	0	3 (12.5 %)	1 (16.7 %)	0	0	2 (33.3 %)
Mild	0	3 (12.5 %)	1 (16.7 %)	0	0	2 (33.3 %)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0
Abdominal distension	0	1 (4.2 %)	0	0	0	1 (16.7 %)
Mild	0	1 (4.2 %)	0	0	0	1 (16.7 %)
Moderate	0	0	0	0	0	0
Severe	0	0	0	0	0	0

The Phase 1 trial was a randomized, double-blind, placebo-controlled study to investigate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of single and multiple ascending doses of DA-1726 in obese, otherwise healthy subjects. The MAD portion of the study enrolled healthy adults with a minimum body mass index between BMI 30 – 45 kg/m^2. The primary endpoint of the Phase 1 trial was to assess the safety and tolerability of DA-1726 by monitoring adverse events (AEs), serious adverse events (SAEs), treatment emergent adverse events (TEAEs) and AEs leading to treatment discontinuation. Secondary endpoints included the PK of DA-1726, assessed via serum concentrations over time and metabolite profiling at the highest doses of DA-1726. Exploratory endpoints included the effect of DA-1726 on metabolic parameters, cardiac parameters, fasting lipid levels, body weight, waist circumference and body mass index (BMI), among others.

For more information on this clinical trial, please visit: www.clinicaltrials.gov NCT06252220.

About DA-1726
DA-1726 is a novel oxyntomodulin (OXM) analogue functioning as a GLP1R/GCGR dual agonist for the treatment of obesity and Metabolic Dysfunction-Associated Steatohepatitis (MASH) that is to be administered once weekly subcutaneously. DA-1726 acts as a dual agonist of GLP-1 receptors (GLP1R) and glucagon receptors (GCGR), leading to weight loss through reduced appetite and increased energy expenditure. DA-1726 has a well understood mechanism and, in pre-clinical mice models, resulted in improved weight loss compared to semaglutide (Wegovy®) and cotadutide (another OXM analogue). Additionally, in pre-clinical mouse models, DA-1726 elicited similar weight reduction, while consuming more food, compared tirzepatide (Zepbound®) and survodutide (a drug with the same MOA), while also preserving lean body mass and demonstrating improved lipid-lowering effects compared to survodutide.

About MetaVia
MetaVia Inc. is a clinical-stage biotechnology company focused on transforming cardiometabolic diseases. The company is currently developing DA-1726 for the treatment of obesity and is developing DA-1241 for the treatment of Metabolic Dysfunction-Associated Steatohepatitis (MASH). DA-1726 is a novel oxyntomodulin (OXM) analogue that functions as a glucagon-like peptide-1 receptor (GLP1R) and glucagon receptor (GCGR) dual agonist. OXM is a naturally-occurring gut hormone that activates GLP1R and GCGR, thereby decreasing food intake while increasing energy expenditure, thus potentially resulting in superior body weight loss compared to selective GLP1R agonists. DA-1241 is a novel G-protein-coupled receptor 119 (GPR119) agonist that promotes the release of key gut peptides GLP-1, GIP, and PYY. In pre-clinical studies, DA-1241 demonstrated a positive effect on liver inflammation, lipid metabolism, weight loss, and glucose metabolism, reducing hepatic steatosis, hepatic inflammation, and liver fibrosis, while also improving glucose control. In a Phase 2a clinical study, DA-1241 demonstrated direct hepatic action in addition to its glucose lowering effects.

For more information, please visit www.metaviatx.com.

Forward Looking Statements
Certain statements in this press release may be considered forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "believes", "expects", "anticipates", "may", "will", "should", "seeks", "approximately", "potential", "intends", "projects", "plans", "estimates" or the negative of these words or other comparable terminology (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. Forward-looking statements are predictions, projections and other statements about future events that are based on current expectations and assumptions and, as a result, are subject to risks and uncertainties. Many factors could cause actual future events to differ materially from the forward-looking statements in this press release, including, without limitation, those risks associated with MetaVia's ability to execute on its commercial strategy; our expectations regarding the sufficiency of our existing cash on hand to fund our operations; the timeline for regulatory submissions; the ability to obtain regulatory approval through the development steps of MetaVia's current and future product candidates; the ability to realize the benefits of the license agreement with Dong-A ST Co. Ltd., including the impact on future financial and operating results of MetaVia; the cooperation of MetaVia's contract manufacturers, clinical study partners and others involved in the development of

MetaVia's current and future product candidates; potential negative interactions between MetaVia's product candidates and any other products with which they are combined for treatment; MetaVia's ability to initiate and complete clinical trials on a timely basis; MetaVia's ability to recruit subjects for its clinical trials; whether MetaVia receives results from MetaVia's clinical trials that are consistent with the results of pre-clinical and previous clinical trials; impact of costs related to the license agreement, known and unknown, including costs of any litigation or regulatory actions relating to the license agreement; the effects of changes in applicable laws or regulations; the effects of changes to MetaVia's stock price on the terms of the license agreement and any future fundraising; and other risks and uncertainties described in MetaVia's filings with the Securities and Exchange Commission, including MetaVia's most recent Annual Report on Form 10-K. Forward-looking statements speak only as of the date when made. MetaVia does not assume any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

Contacts:

MetaVia
Marshall H. Woodworth
Chief Financial Officer
+1-857-299-1033
marshall.woodworth@metaviatx.com

Rx Communications Group
Michael Miller
+1-917-633-6086
mmiller@rxir.com

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