MetaVia Announces Positive Top-Line Results From Its Phase 2a Clinical Trial of DA-1241 in Patients with Presumed MASH

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- *DA-1241 Demonstrated Direct Hepatic Action in Addition to Its Glucose Lowering Effect*
- *Patients Treated with DA-1241 100mg Achieved Statistically Significant Reduction in ALT Levels at Weeks 4 and 8, and a Near Statistically Significant Reduction at Week 16*
- *DA-1241 100mg Demonstrated Statistically Significant Improvements in CAP Score at Week 16*
- *DA-1241 100mg Showed Statistically Significant Reductions in HbA1C at Week 16*
- *DA-1241 was Very Well Tolerated*
- *Awaiting Data on Other Exploratory Endpoints Including MRI-PDFF*
- *Additional Findings to be Submitted for Upcoming Scientific Conferences*

CAMBRIDGE, Mass., Dec. 18, 2024 /PRNewswire/ -- **MetaVia Inc.** (Nasdaq: MTVA), a clinical-stage biotechnology company focused on transforming cardiometabolic diseases, today announced positive top-line 16-week results from the two-part Phase 2a clinical trial in patients with presumed metabolic dysfunction-associated steatohepatitis (MASH). Part 1 of this Phase 2a trial is exploring DA-1241, a novel G-Protein-Coupled Receptor 119 (GPR119) agonist compared to placebo, while Part 2 is investigating the efficacy of DA-1241 in combination with sitagliptin, a DPP-4 inhibitor. In this trial, DA-1241 (100mg) demonstrated a statistically significant reduction in alanine transaminase (ALT) levels at weeks 4 and 8, with a near statistically significant reduction at week 16. Statistically significant results were also achieved in multiple secondary endpoints including reductions in controlled attenuation parameter (CAP) and hemoglobin A1C (HbA1c) (see tables below). DA-1241 demonstrated similar trends in other liver enzymes including aminotransferase (AST) and gamma-glutamyl transferase (GGT).

Primary Efficacy Endpoint

LS Mean ALT Changes from Baseline (U/L)

	Placebo (N=23)	**DA-1241 100mg + Sitagliptin 100mg (N=34)**	P value vs. PBO	**DA-1241 50mg (N=12)**	P value vs. PBO	**DA-1241 100mg (N=22)**	P value vs. PBO
Baseline Mean	68.4	63.2		65.8		57.2	
Week 4 LS Mean (95% CI)	-1.51 (-8.23, 5.21)	-8.38 (-13.89, -2.87)*	0.1195	-9.63 (-18.90, -0.35)*	0.1622	-13.44 (-20.32, -6.57)*	0.0159†
Week 8 LS Mean (95% CI)	0.13 (-7.83, 8.09)	-10.27 (-16.80, -3.73)*	0.0479†	-11.05 (-22.04, -0.05)*	0.1050	-12.25 (-20.40, -4.10)*	0.0342†
Week 16 LS Mean (95% CI)	-4.70 (-14.05, 4.65)	-8.24 (-15.91, -0.57)*	0.5624	-16.81 (-29.72, -3.89)*	0.1345	-18.09 (-27.67, -8.52)*	0.0506

* Confidence interval excludes 0, suggesting a statistically meaningful difference.
† p < 0.05 vs. placebo

Notable Secondary Endpoints

Proportion of Subjects with Normalized ALT <30 IU/L at Week 16

	Placebo (N=23)	**DA-1241 100mg + Sitagliptin 100mg (N=34)**	**DA-1241 50mg (N=12)**	**DA-1241 100mg (N=22)**
Number of Subjects, n				
< 30, n (%)	1 (4.3 %)	3 (8.8 %)	4 (33.3 %)	4 (18.2 %)
Odds Ratio (p value)		2.423 (0.4576)	10.500 (0.0487)†	5.600 (0.1402)

† p < 0.05 vs. placebo

LS Mean CAP, VCTE, FAST score Changes from Baseline at Week 16

	Placebo (N=23)	DA-1241 100mg + Sitagliptin 100mg (N=34)	P value vs. PBO	DA-1241 50mg (N=12)	P value vs. PBO	DA-1241 100mg (N=22)	P value vs. PBO
Baseline Mean (dB/m)	347.4	344.1		347.3		336.0	
Week 16 LS Mean CAP Score (dB/m) (95% CI)	-2.32 (-16.17, 11.52)	-20.62 (-31.99, -9.26)*	0.0452†	-8.94 (-28.08, 10.20)	0.5787	-24.32 (-38.54, -10.10)*	0.0308†
Baseline Mean (kPa)	10.00	9.89		10.71		10.32	
Week 16 LS Mean VCTE Score (kPa) (95% CI)	0.29 (-1.31, 1.89)	-1.45 (-2.77, -0.13)*	0.0997	-1.40 (-3.62, 0.83)	0.2257	0.00 (-1.64, 1.64)	0.8051
Baseline Mean	0.555	0.564		0.604		0.538	
Week 16 LS Mean FAST score (95% CI)	-0.09 (-0.17, -0.01)*	-0.19 (-0.26, -0.13)*	0.0416†	-0.17 (-0.28, -0.06)*	0.2429	-0.19 (-0.27, -0.11)*	0.0704

* Confidence interval excludes 0, suggesting a statistically meaningful difference.
† p < 0.05 vs. placebo

LS Mean HbA1C Changes from Baseline at Week 16 (%)

	Placebo (N=23)	DA-1241 100mg + Sitagliptin 100mg (N=34)	P value vs. PBO	DA-1241 50mg (N=12)	P value vs. PBO	DA-1241 100mg (N=22)	P value vs. PBO
Baseline Mean	6.78	6.51		6.58		7.01	
Week 16 LS Mean (95% CI)	-0.10 (-0.23, 0.44)	-0.52 (-0.80, -0.25)*	0.0050†	-0.24 (-0.70, 0.22)	0.2357	-0.48 (-0.82, -0.13) *	0.0179†

* Confidence interval excludes 0, suggesting a statistically meaningful difference.
† p < 0.05 vs. placebo

Overall TEAE Summary

N (%)	Placebo (N=32)	DA-1241 100mg + Sitagliptin 100mg (N=36)	DA-1241 50mg (N=14)	DA-1241 100mg (N=26)
Subjects with any Treatment Related AE	9 (28.1%)	10 (27.8%)	4 (28.6%)	9 (34.6%)
Mild	8 (25.0%)	9 (25.0%)	4 (28.6%)	8 (30.8%)
Moderate	1 (3.1%)	1 (2.8%)	0	1 (3.8%)
Severe	0	0	0	0
Subjects with any Treatment related SAE	0	0	0	0
Subjects with any TEAE leading to study discontinuation	0	1 (3.1 %)	0	0
Subjects with any TEAE leading to study drug discontinuation	1 (3.1 %)	0	0	0

- DA-1241 100mg showed statistically significant reductions in ALT levels at weeks 4 and 8 (p=0.0159 and p=0.0342, respectively) and a near statistically significant reduction (p=0.0506) at week 16 compared to placebo.
- DA-1241 50mg showed a statistically significant improvement in the normalization of ALT levels compared to placebo, with an odds ratio of 10.500 (p=0.0487).
- DA-1241 100mg and DA-1241 100mg + Sitagliptin 100mg showed significant improvements in the CAP score compared to placebo (p=0.0308 and p=0.0452, respectively).
- DA-1241 100mg + Sitagliptin 100mg showed a statistically significant reduction in the FAST score compared to placebo (p=0.0416).
- DA-1241 100mg and DA-1241 100mg + Sitagliptin 100mg showed significant reductions in HbA1C from baseline at Week 16 compared to the placebo group (p=0.0179 and p=0.0050, respectively).

"Achieving the primary endpoint of a reduction in ALT levels through direct hepatic effects, as well as notable secondary endpoints, including significantly lower HbA1C levels compared to the placebo, are extremely positive results for DA-1241, especially given the small study size," stated Hyung Heon Kim, President and Chief Executive Officer of MetaVia. "Importantly,

DA-1241 was shown to be very well tolerated with mostly mild AEs and no drug related SAEs in the treatment groups. Based on this data, we continue to believe that the novel mechanism of action of DA-1241, addressing the inflammation linked to MASH, will result in a safe and effective treatment option for this disease. We continue to conduct pre-clinical studies to explore other combination therapies for DA-1241, which may provide additional benefits to treat patients along the full spectrum on MASH. We look forward to the full data set and expect to have an end of Phase 2 meeting with the U.S. Food and Drug Administration (FDA) in the first half of 2025."

Each of the two parts of the Phase 2a trial of DA-1241 were designed to be 16-week, multicenter, randomized, double-blind, placebo-controlled, parallel clinical studies to evaluate the efficacy and safety of DA-1241 in subjects with presumed MASH. A total of 109 patients were randomized, while 95 patients completed the dosing. These patients were enrolled in either Part 1, which is exploring the efficacy of DA-1241 versus placebo, and randomized in a 1:2:1 ratio into 3 treatment groups: DA-1241 50 mg, DA-1241 100mg or placebo, or into Part 2, which is exploring the efficacy of DA-1241 in combination with sitagliptin versus placebo, randomized in a 2:1 ratio into 2 treatment groups: DA-1241 100mg/sitagliptin 100mg or placebo. For both Part 1 and Part 2, the primary endpoint is the change from baseline in alanine transaminase (ALT) levels at Week 16.

For more information on this clinical trial, please visit: www.clinicaltrials.gov NCT06054815.

About DA-1241
DA-1241 is a novel G-Protein-Coupled Receptor 119 (GPR119) agonist with development optionality as a standalone and/or combination therapy for both MASH and type 2 diabetes (T2D). Agonism of GPR119 in the gut promotes the release of key gut peptides GLP-1, GIP, and PYY. These peptides play a further role in glucose metabolism, lipid metabolism and weight loss. DA-1241 has beneficial effects on glucose, lipid profile and liver inflammation, supported by potential efficacy demonstrated during in vivo preclinical studies. The therapeutic potential of DA-1241 has been demonstrated in multiple pre-clinical animal models of MASH and T2D where DA-1241 reduced hepatic steatosis, inflammation, fibrosis, and improved glucose control. Furthermore, in Phase 1a and 1b trials, DA-1241 was well tolerated in both healthy volunteers and those with T2DM.

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.

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; 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.

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