MetaVia Presents Pre-Clinical Data on DA-1241 Demonstrating Additive Hepatoprotective Effects in Combination With Efruxifermin at the ADA's 85th Scientific Session

June 21, 2025

CAMBRIDGE, Mass., June 21, 2025 /PRNewswire/ -- **MetaVia Inc.** (Nasdaq: MTVA), a clinical-stage biotechnology company focused on transforming cardiometabolic diseases, today announced the presentation of pre-clinical data on DA-1241, a novel G-Protein-Coupled Receptor 119 (GPR119) agonist, demonstrating additive hepatoprotective effects in combination with Efruxifermin, a fibroblast growth factor 21 (FGF21) analogue, in a metabolic dysfunction-associated steatohepatitis (MASH) mouse model. The data will be presented in a poster session, tomorrow, at the American Diabetes Association's 85th Scientific Sessions, taking place June 20-23, 2025, at the McCormick Place Convention Center in Chicago, Illinois.

"Building on the encouraging results from our Phase 2a clinical trial of DA-1241 in patients with presumed MASH, which demonstrated hepatoprotective and glucose-regulating effects, these new preclinical findings presented at the ADA further highlight the promise of combining DA-1241 with an FGF21 analogue like Efruxifermin," stated Hyung Heon Kim, President and Chief Executive Officer of MetaVia. "This combination therapy demonstrated, for the first time, beneficial synergistic effects in reducing liver fat, inflammation, and fibrosis, all key drivers of MASH progression. This reinforces our belief in the therapeutic potential of DA-1241 as part of a combination strategy to address the complex pathology of MASH."

The pre-clinical study was conducted with mice fed a Gubra Amylin NASH (GAN) diet for 36 weeks to induce advanced liver pathology consistent with human MASH. Mice were then randomized to receive either vehicle, DA-1241 (100 mg/kg once daily, oral), Efruxifermin (EFX) (1 mg/kg once weekly, subcutaneous), or the combination therapy for 12 weeks.

DA-1241 was found to be weight-neutral over the 12-week treatment period, while EFX monotherapy induced a statistically significant 17% reduction in body weight compared to vehicle ($p < 0.05$). No additional weight loss was observed with the combination therapy, indicating that further benefits induced by the combination were independent of weight loss. Both DA-1241 and EFX monotherapies led to improvements in liver function markers, including reductions in plasma transaminases and hepatic cholesterol levels. Notably, the combination therapy produced greater improvements in these biomarkers than either agent alone, suggesting an additive hepatoprotective effect. Histological analysis demonstrated that 94% of mice receiving the combination therapy achieved a ≥2-point improvement in the non-alcoholic fatty liver disease (NAFLD) activity score from baseline, compared to lower response rates observed with either monotherapy, underscoring the enhanced therapeutic potential of the combined regimen. Further, liver lipid area and steatotic hepatocytes also decreased more with the combination therapy.

Liver immunohistochemistry revealed significantly reduced inflammatory (galectin-3) and fibrotic (type 1 collagen and α-SMA) proteins in the liver, suggesting enhanced effects over monotherapy. In line with this, liver mRNA analysis showed marked decreases in inflammatory (TNFα -58%, CXCL10 -56%, CCL2 -77%, galectin-3 -87%) and fibrotic (type 1 collagen α1 -72%, α-SMA -59%, TIMP1 -88%) gene expression in the combination. Notably, hedgehog-interacting protein, a suppressor of hepatic stellate cell activation, was upregulated more (+321%) in the combination than in each alone. Moreover, this combination further reduced plasma TNFα levels, suggesting further improvement in, not only local inflammation, but also systemic inflammation. These findings suggest that combining two drugs with different mechanisms of action, but which act directly on the liver, can provide additional therapeutic benefits in improving MASH pathology.

Presentation Details:

- **Title:** *Additive Hepatoprotective Effects of DA-1241, a GPR119 Agonist, in Combination with Efruxifermin in a Diet-Induced Obese and Biopsy-Confirmed Mouse Model of MASH*
- **Presenting Author:** Yuna Chae, Lead Research Scientist, Dong-A ST Research Center
- **Abstract Control Number:** 2158-LB
- **Session:** 22-C Integrated Physiology—Liver
- **Presentation Date:** Sunday, June 22, 2025
- **Presentation Time:** 12:30-1:30 pm CT

A copy of the poster will be available on the Posters section of the MetaVia website after the presentation. Additionally, the poster will be published online on the journal, Diabetes®, website.

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, 1b and 2a trials, DA-1241 was well tolerated in both healthy volunteers and those with T2DM. In a Phase 2a clinical study, DA-1241 demonstrated direct hepatic action in addition to its glucose lowering effects.

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. In a Phase 1 multiple ascending dose (MAD) trial in obesity, DA-1726 demonstrated best-in-class potential for weight loss, glucose control, and waist reduction. 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.

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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