

Media Release

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Aprocitentan efficacy data reinforce endothelin pathway blockade as a distinct therapeutic approach across the cardiometabolic disease spectrum including obesity

Two oral presentations at AHA Hypertension 2026 demonstrate the pronounced efficacy of aprocitentan in two groups of patients with notoriously difficult to control hypertension from the PRECISION study: patients with obesity and patients across the cardiovascular-kidney-metabolic (CKM) continuum.

In both groups of patients, aprocitentan induced a rapid double-digit reduction in blood pressure and was associated with improved UACR and stable renal function, suggesting a potential kidney protective effect. A trend towards improvement was also observed in several metabolic biomarkers.

The robust effects observed in patients with obesity or CKM disease further underscore the importance of blocking the upregulated endothelin system in difficult-to-control hypertension.

Allschwil, Switzerland – October 12, 2026

Idorsia Ltd (SIX: IDIA) shared positive findings from two new analyses of the pivotal Phase 3 PRECISION study of aprocitentan in patients with resistant hypertension, at the American Heart Association Hypertension Scientific Sessions 2026 on October 10.

Amer Joseph, MD, Chief Medical Officer and Head of Global Clinical Development

“For us, these results are an important step in understanding where targeting the endothelin pathway makes the greatest difference for patients with uncontrolled hypertension. In PRECISION, aprocitentan produced a double-digit blood pressure reduction in the overall population. We are encouraged to see consistent blood pressure reductions in patients with obesity and across earlier and more advanced stages of CKM, given their complex and overlapping clinical risks. Together with the reduction in UACR, stable eGFR and safety profile, this adds to the growing evidence that the endothelin pathway matters in patients across the broader spectrum of uncontrolled hypertension.”

An estimated 1.4 billion people worldwide live with hypertension, yet many do not achieve adequate control, increasing their risk of cardiovascular and kidney complications and premature death.¹ The burden is particularly high among people with obesity or CKM.²⁻⁴

A 5-10 mmHg reduction in systolic blood pressure can reduce the risk of major cardiovascular events by approximately 10%-20%.⁵ Yet, despite the well-established benefits of lowering blood pressure, many patients remain above target despite multiple therapies, underscoring the need for treatments that address additional pathways involved in hypertension.

When the endothelin system is upregulated, endothelin-1 drives vasoconstriction, vascular and cardiac hypertrophy, fibrosis, inflammation and aldosterone production. It is especially the case in populations prone to difficult-to-control hypertension such as obesity, type 2 diabetes, and renal failure. There is a strong correlation between ET-1 and markers of metabolic syndrome (body mass index, triglycerides, insulin resistance), and between ET-1 and kidney function. By blocking ETA and ETB receptors, aprocitentan targets this distinct pathway beyond the renin-angiotensin-aldosterone system.^{6,7}

Aprocitentan shows marked benefits in patients with obesity and hypertension

- **Endothelin is a driver of hypertension in individuals with obesity: A post hoc analysis of the PRECISION study. Presented by Dr Michael A Weber, MD**
Markus Schlaich, Martine Clozel, Ruth Collins, Parisa Danaïetash, John M. Flack, Johann Laurent, Krzysztof Narkiewicz, Ji-Guang Wang and Michael A Weber.
[Abstract available online](#)

This post hoc analysis compared 506 patients with obesity defined as body mass index ≥ 30 kg/m² with 224 patients without obesity. At baseline, office blood pressure was similar between groups, while patients with obesity carried a higher burden of several comorbidities, including diabetes, chronic kidney disease, ischemic heart disease, congestive heart failure and obstructive sleep apnea.

Key findings:

- Aprocitentan 12.5 mg and 25 mg reduced office systolic blood pressure at Week 4 in patients with obesity by 15.4 and 16.0 mmHg respectively, consistent with the reduction observed in the overall PRECISION population. Double-digit absolute reductions were maintained during the 32-week single-blind treatment period to Week 36.
- Night-time ambulatory systolic blood pressure decreased in patients with obesity, with the reduction maintained during longer-term treatment.
- UACR decreased in patients with obesity, eGFR remained stable while uric acid showed favorable changes with aprocitentan versus placebo.
- Safety profile was consistent between the two cohorts

Dr. Michael A. Weber, Professor of Medicine at the SUNY Downstate College of Medicine in Brooklyn, New York, commented:

"Obesity and hypertension are major, interconnected drivers of cardiovascular risk. As the endothelin pathway is upregulated in uncontrolled hypertension and adipose tissue can contribute to endothelin production, it represents a compelling therapeutic target in patients with obesity and resistant hypertension. In this post hoc analysis of PRECISION, aprocitentan substantially reduced office systolic blood pressure in patients with obesity, consistent with the double-digit reduction observed in the overall PRECISION population and was also associated with signs of kidney protection, a vital objective in this population. These findings reinforce the role of the endothelin pathway in obesity-associated resistant hypertension."

Aprocitentan showed marked benefits in patients with CKM and hypertension

- **Endothelin as a therapeutic target across the cardiovascular-kidney-metabolic continuum: A post hoc analysis of the PRECISION study. Presented by Dr John M. Flack**
Markus Schlaich, Martine Clozel, Parisa Danaïetash, Johann Laurent, Alessandro Maresta, Krzysztof Narkiewicz, Ji-Guang Wang, Michael A Weber and John M. Flack.
[Abstract available online](#)

This post hoc analysis focused on 410 patients in CKM stage 2 and 273 patients in CKM stage 4a. Patients in stage 4a were older and had a greater burden of diabetes, chronic kidney disease, ischemic heart disease, heart failure and cerebrovascular disease, while baseline office and ambulatory blood pressure were similar between cohorts.

Key findings:

- Aprocitentan 12.5 mg reduced office systolic blood pressure at Week 4, by 15.1 mmHg in patients with CKM stage 2 and by 16.6 mmHg in those with stage 4a.

- At Week 4, daytime and night-time ambulatory systolic blood pressure decreased in both CKM cohorts.
- Increase of the UACR is associated with higher risks of mortality in patients with CKM.⁸ Aprocitentan reduced UACR by almost 50% across earlier and more advanced CKM stages in patients with albuminuria. Urate showed also favorable trends versus placebo in both CKM cohorts.
- Estimated glomerular filtration rate remained stable over the duration of the study in both cohorts. NT-proBNP was also stable, and no increase in electrolyte abnormalities was observed.
- The safety profile was consistent between CKM stages 2 and 4a.

Dr. John M. Flack, Professor and Chair of the Departments of Medicine and Population Science at Southern Illinois University School of Medicine, commented:

“Patients with hypertension across the CKM spectrum face a considerable burden of morbidity and mortality. The risk of cardiovascular death increases markedly with CKM progression, nearly tripling from earlier stages to stage 4. Since endothelin is implicated in blood pressure regulation, kidney function, adiposity and other CKM-related processes, we wanted to understand whether blocking this pathway could provide consistent benefits across different stages of CKM. Aprocitentan substantially reduced blood pressure, consistent with the double-digit reduction observed in the overall PRECISION population. Importantly, it also reduced UACR by approximately 50% across both earlier and more advanced CKM stages. Knowing that an increase of UACR is associated with a higher risk of all-cause and cardiovascular-related mortality, these findings highlight the potential importance of targeting the endothelin system in uncontrolled hypertension.”

Notes to the editor

About Dr Michael A. Weber, MD

Dr. Weber is Professor of Medicine at the SUNY Downstate College of Medicine in Brooklyn, New York. He received his medical degree from Sydney University in Australia. His career has been focused primarily on hypertension and preventive cardiology. He has published numerous research articles in medical literature and has authored or edited several books.

Dr. Weber was the Editor-in-Chief of The Journal of Clinical Hypertension for over 10 years. Dr. Weber was one of the founders of The American Society of Hypertension and has served as its President. He also served as Chair of the ASH Hypertension Specialists Program. He is a Fellow of The American College of Physicians, The American College of Cardiology and The American Heart Association. He has served on the Cardiovascular and Renal Drugs Advisory Board of the Food and Drug Administration. He has also served for ten years as Chairman of the Formulary Committee of a major pharmacy benefits provider serving many of the leading health plans in the United States.

His main current research interests are in clinical trials of patients at high risk of cardiovascular events or strokes. He is also participating actively in trials in patients with metabolic disorders such as diabetes and kidney disease. Dr. Weber currently serves on the Steering Committees of several national and international clinical trials. Dr. Weber serves as a consultant to Idorsia.

About Dr. John M. Flack, MD

Dr. Flack, an Alpha Omega Alpha (AOA) graduate of the University of Oklahoma School of Medicine, is the Sergio Rabinovich Endowed Chair of Internal Medicine and the Professor and Chair of the Departments of Medicine and Population Science at Southern Illinois University School of Medicine. He is also Director of the Hypertension Clinic.

He is a board-certified Internal Medicine specialist and an internationally renowned hypertension specialist/cardiovascular epidemiologist with widely recognized clinical/research expertise in hypertension in African Americans, resistant/refractory hypertension, device-based therapies for hypertension and racial cardiovascular health disparities. Dr. Flack is the current President of the American Hypertension Specialist Certification Program. He has published over 250 peer-reviewed manuscripts and book chapters and is an Associate Editor for the journal Hypertension. He maintains an active clinical practice in complex

hypertension at SIU where he teaches and mentors medical students and residents and undertakes innovative, cutting-edge research.

Dr. Flack has received numerous awards including the Distinguished Research Award (1993) from the International Society on Hypertension in Blacks (ISHIB), the Daniel D. Savage Memorial Scientific Award (1998) from the Association of Black Cardiologists (ABC), the F. Dewey Dodrill Award for Excellence (2007) from the American Heart Association (AHA), the Detroit News Michigania of the Year (2009), and the University of Oklahoma Academic Physician of the Year (2012). Also, he has been repeatedly named to Top Doctor, Best Doctor, and Super Doctor lists. Previously, he served as a voting member of the FDA Cardio-Renal Advisory Board. Dr. Flack was recently conferred the status of Master by the American College of Physicians (ACP); he also previously served as a member of the ACP Board of Regents. Dr. Flack serves as a consultant to Idorsia.

About aprocitentan

Aprocitentan is a once-daily, orally active, dual endothelin receptor antagonist, which inhibits the binding of ET-1 to ETA and ETB receptors. Aprocitentan is approved as **TRYVIO®** in the US for the treatment of systemic hypertension in combination with other antihypertensive drugs, to lower blood pressure in adult patients who are not adequately controlled on other drugs, and has been commercially available since October 2024. For more information see the Full Prescribing Information including BOXED Warning ([PI](#) and [Medication Guide](#)). TRYVIO is now included in the American College of Cardiology's (ACC) and the American Heart Association's (AHA) new comprehensive clinical practice guidelines for the management of high blood pressure. Aprocitentan is approved as **JERAYGO™** for the treatment of resistant hypertension in combination with other antihypertensives in the European Union, the UK, Switzerland, and Canada.

About PRECISION^{9,10} (NCT03541174)

PRECISION was a multicenter, blinded, randomized, parallel-group, Phase 3 study, which was performed in Europe, North America, Asia, and Australia. Patients were eligible for randomization if their sitting systolic blood pressure was 140 mm Hg or higher despite taking standardized background therapy consisting of three antihypertensive drugs, including a diuretic. The study consisted of three sequential parts: Part 1 was the 4-week double-blind, randomized, and placebo-controlled part, in which 730 patients were randomized to aprocitentan 12.5 mg (n=243), aprocitentan 25 mg (n=243), or placebo (n=244) in a 1:1:1 ratio; Part 2 was a 32-week single (patient)-blind part, in which all patients received aprocitentan 25 mg (n=704); and Part 3 was a 12-week double-blind, randomized, and placebo-controlled withdrawal part, in which patients were re-randomized to aprocitentan 25 mg (n=307) or placebo (n=307) in a 1:1 ratio. The primary and key secondary endpoints were changes in unattended office systolic blood pressure from baseline to week 4 and from withdrawal baseline to week 40, respectively. Secondary endpoints included 24-h ambulatory blood pressure changes.

At baseline, 69.2% of patients were obese or severely obese, 54.1% had diabetes, 22.2% had stage 3-4 chronic kidney disease and 19.6% had congestive heart failure. 63% of randomized patients were receiving at least 4 anti-hypertensive therapies at screening.

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About Idorsia

The purpose of Idorsia is to discover, develop and commercialize innovative medicines to help more patients. To achieve this, we will develop Idorsia into a leading biopharmaceutical company, with a strong scientific core.

Headquartered near Basel, Switzerland – a European biotech hub – Idorsia has a highly experienced team of dedicated professionals, covering all disciplines from bench to bedside; QUVIVIQ™ (daridorexant), a different kind of insomnia treatment with the potential to revolutionize this mounting public health concern; strong partners to maximize the value of our portfolio; a promising in-house development pipeline; and a specialized drug discovery engine focused on small-molecule drugs that can change the treatment paradigm for many patients. Idorsia is listed on the SIX Swiss Exchange (ticker symbol: IDIA).

For further information, please contact:

Investor & Media Relations

Idorsia Pharmaceuticals Ltd, Hegenheimermattweg 91, CH-4123 Allschwil

+41 58 844 10 10

investor.relations@idorsia.com - media.relations@idorsia.com - www.idorsia.com

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