# Media Release
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## New Hypertension publication underscores aprocitentan's potential in managing hypertension patients with CKD

- New analysis from landmark Phase 3 PRECISION trial published in *Hypertension* highlights the renal-protective benefits of aprocitentan in addition to the marked reduction in blood pressure in a high-risk CKD population with difficult-to-control hypertension

**Allschwil, Switzerland – December 10, 2025**
Idorsia Ltd (SIX: IDIA) announced the publication of a new analysis from the landmark Phase 3 PRECISION study in *Hypertension* titled "Aprocitentan in Patients with Chronic Kidney Disease and Resistant Hypertension".[1] The analysis examined the efficacy and safety of aprocitentan (TRYVIO™/JERAYGO™) in patients with chronic kidney disease (CKD) and confirmed resistant hypertension – a population with very limited treatment options and high cardiovascular and renal risk.

Aprocitentan, the first approved antihypertensive targeting the endothelin pathway, was well tolerated. It significantly reduced both office and nighttime ambulatory blood pressure (BP), as well as markedly lowered albuminuria – a key marker of kidney damage – without increasing the risk of hyperkalemia.

**Patrick Rossignol, MD, PhD, nephrologist, Head of the Medical Specialties and nephrology departments at the Princess Grace Hospital, Monaco, commented:**
"Hypertension is both a cause and consequence of chronic kidney disease (CKD) and managing it in these patients is particularly challenging. Blood pressure is often difficult to control, and many antihypertensive agents carry risks of worsening renal function or causing hypo or hyperkalemia, which are all associated with dismal outcomes. The data presented in this manuscript are truly transformative for our patients: aprocitentan not only markedly lowered blood pressure but also reduced proteinuria by up to 60% on top of standardized background triple therapy including valsartan and a thiazide-like diuretic – without inducing dyskalemia or worsening renal function. Its favorable safety profile and exceptionally low discontinuation rate after nearly one year of treatment position aprocitentan as a fundamental advancement for patients with CKD and treatment resistant hypertension."

**Martine Clozel, MD, Chief Scientific Officer and Head of Research at Idorsia, commented:**
"The PRECISION study included patients with confirmed resistant hypertension without excluding patients with stage 3 or 4 chronic kidney disease (CKD), as these patients are particularly underserved. The endothelin pathway plays a clear role in both kidney dysfunction and hypertension, yet until aprocitentan, no antihypertensive therapy targeted this pathway – explaining why many patients were not responding to treatment. TRYVIO/JERAYGO blocks the two endothelin receptor subtypes fundamental in its actions. In patients who had often tried more than four antihypertensive drugs, aprocitentan delivered significant blood pressure reductions alongside a major antiproteinuric effect, suggesting meaningful renal protection."

There are 1.4 billion people worldwide living with hypertension.[2] Hypertension remains a leading global health challenge and the number one modifiable risk factor for early morbidity and mortality. Despite advances in treatment, many patients still struggle with uncontrolled blood pressure, leaving them at significantly higher risk of heart attack, stroke, kidney failure, and premature death.[3] In the US, approximately 50% of patients living with hypertension on multiple treatments do not have their blood pressure under control.[4]

In patients with CKD, hypertension significantly contributes to preventable morbidity and mortality and is a leading cause of cardiovascular disease.[5-7] In 2019, there were more than 650 million people with CKD worldwide and 1.2 million deaths due to CKD.[8] Especially nocturnal hypertension has been associated with increased cardiovascular morbidity.[9-11] Therefore, appropriate and effective management of hypertension is a key strategy of managing patients with CKD.[12,13]

Endothelin-1 (ET-1) is a potent vasoconstrictor that also induces neurohormonal activation, vascular hypertrophy and remodeling, cardiac hypertrophy and fibrosis, and endothelial dysfunction. In hypertension, both $ET_A$ and $ET_B$ receptors mediate harmful effects of ET-1.[14] As a vasoconstrictor, co-mitogenic agent, linking pulse pressure and vascular remodeling, and mediator of aldosterone and catecholamine release, endothelin is a key player in hypertension and end-organ damage.[15,16]

Upregulation of endothelin-1 is considered an important contributor to the pathophysiology of CKD progression, including increased blood pressure, glomerular membrane permeability, mesangial cell proliferation, podocyte dysfunction, interstitial inflammation and fibrosis.[17,18]

## About the analysis[1]

The Phase 3 PRECISION study evaluated aprocitentan in 730 patients with confirmed resistant hypertension. This post-hoc analysis focused on the 147 participants with CKD categorized as high or very high risk according to KDIGO criteria.[19]

- At Week 4, aprocitentan 12.5 mg and 25 mg reduced office systolic BP by –13.5 mm Hg and –16.6 mm Hg, respectively, versus –4.4 mm Hg with placebo – with reductions sustained with aprocitentan 25 mg through Week 36 (-16.4 mm Hg)
- Nighttime ambulatory systolic BP – a strong predictor of cardiovascular and renal outcomes and often poorly controlled in CKD – was reduced by –9.6 mm Hg and –13.8 mm Hg, respectively, versus –2.5 mm Hg with placebo.
- UACR – a marker of kidney damage and progression – was reduced by –47.1% and –59.6%, respectively, versus –2.4% with placebo – with reductions associated with improved long-term prognosis sustained through Week 36 (–61.6%).
- Aprocitentan was generally well tolerated. The most common adverse event was mild-to-moderate peripheral edema, typically seen early on and managed with diuretic adjustment. No significant changes in potassium or estimated glomerular filtration rate (eGFR) were observed.

## About aprocitentan

Aprocitentan is Idorsia's 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 antihypertensives 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, and Switzerland, and a marketing authorization application is under review in Canada.

## About PRECISION[20,21] (NCT03541174)

PRECISION was a multicenter, blinded, randomized, parallel-group, Phase 3 study, which was performed in hospitals or research centers 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.

## Key PRECISION findings[21]

The least square mean change in office SBP at 4 weeks was –15.3 mmHg for aprocitentan 12.5 mg, –15.2 mmHg for 25 mg, and –11.5 mmHg for placebo, for a difference versus placebo of –3.8 mmHg (p=0.0042) and –3.7 mmHg (p=0.0046), respectively. Office diastolic blood pressure (DBP) also decreased with both aprocitentan doses compared to placebo (–3.9 mmHg for the 12.5 mg dose and –4.5 mmHg for the 25 mg dose). Office SBP and DBP were maintained during Part 2 in patients previously receiving aprocitentan and decreased within the first 2 weeks of Part 2 before stabilizing in those previously receiving placebo. In Part 3, office SBP after 4 weeks of withdrawal (the key secondary endpoint) increased significantly with placebo compared to aprocitentan (5.8 mmHg; p<0.0001). Office DBP also increased with placebo compared to aprocitentan (5.2 mmHg; p<0.001). The difference between the two groups remained up to week 48.

The results from ambulatory BP monitoring, a strong predictor of cardiovascular mortality,[1,2] confirmed those derived from office measurements. At the end of Part 1, aprocitentan, after placebo correction, decreased both the 24-hour ambulatory SBP (–4.2 mmHg for the 12.5 mg dose and –5.9 mmHg for the 25 mg dose) and DBP (–4.3 mmHg for the 12.5 mg dose and –5.8 mmHg for the 25 mg dose). The placebo-corrected SBP lowering effect was –5.1 mmHg and –7.4 mmHg during the nighttime and –3.8 mmHg and –5.3 mmHg during the daytime, for the 12.5 mg and 25 mg doses, respectively. In Part 3, after 4 weeks of withdrawal (week 40), both the 24-hour ambulatory SBP and DBP increased with placebo compared with aprocitentan (6·5 mm Hg and 6·8 mm Hg respectively).

Treatment-emergent adverse events (TEAEs) during the 4-week double-blind study period (Part 1) were reported in 27.6% and 36.7% of the patients treated with 12.5 and 25 mg aprocitentan, respectively, versus 19.4% in the placebo group. The most frequent adverse event was fluid retention which was reported more frequently with aprocitentan than with placebo in a dose-dependent fashion (9.1%, 18.4%, and 2.1% for patients receiving aprocitentan 12.5 mg, 25 mg and placebo, during Part 1, respectively; 18.2% for patients receiving aprocitentan 25 mg during Part 2; and 2.6% and 1.3% for patients on aprocitentan 25 mg and placebo, during Part 3, respectively). Fluid retention was generally mild-to-moderate, was primarily peripheral edema and was manageable by current

clinical practice including use of diuretics. Discontinuation due to edema/fluid retention was reported for seven patients.

## Notes to the editor

### About Dr Patrick Rossignol, MD, PhD

Patrick Rossignol is a nephrologist and vascular medicine specialist, European Society of Hypertension-certified hypertension specialist and formerly a Professor of Therapeutics at the University of Lorraine, France.

Since 2022, he is heading the Department of Medicine specialties and nephrology-hemodialysis at the Princess Grace Hospital, in Monaco. He is also the medical director of the private hemodialysis Centre, in Monaco. He is chairing Monaco Clinical Research Infrastructure Network (M-CRIN) since its creation in 2025.
He is the Coordinator of the FCRIN INI-CRCT (Cardiovascular and Renal Clinical trialists network of excellence www.inicrct.fr,) since its creation 2014, FCRIN being the "French Clinical research Infrastructure network".

From 2018 to 2022, he used to be the Director of the Nancy University Hospital INSERM Clinical Investigation Centre, after serving as its Deputy Director for ten years. He is now an associate researcher. He is also the Kidney Disease Clinical Trialists (KDCT) workshop course director.

Professor Rossignol has been involved in numerous clinical trials in the settings of heart failure, hypertension and chronic kidney disease as well as in translational basic research studies on the cardiorenal syndrome. He has published more than 700 peer-reviewed publications and is co-inventor of 9 biomarker international patents in the cardiorenal syndrome setting.

Prof Rossignol used to serve as a consultant to Idorsia while he was chairing the PRECISION trial critical event committee.

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**About Idorsia**

Idorsia Ltd is reaching out for more – we have more passion for science, we see more opportunities, and we want to help more patients.

The purpose of Idorsia is to challenge accepted medical paradigms, answering the questions that matter most. To achieve this, we will discover, develop, and commercialize transformative medicines – either with in-house capabilities or together with partners – and evolve 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).

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