Media Release
April 9, 2025

The effect of aprocitentan for reducing blood pressure and proteinuria in Black patients with resistant hypertension published in Hypertension

- Aprocitentan, on top of background therapy, showed clinically meaningful and durable blood pressure (BP) reduction and a decrease in proteinuria in Black patients with confirmed resistant hypertension

Allschwil, Switzerland – April 9, 2025
Idorsia Ltd (SIX: IDIA) today announced the publication of "Aprocitentan for Blood Pressure Reduction in Black Patients" in the April edition of *Hypertension*[1]. The publication reports preplanned analyses of the efficacy, tolerability and safety of aprocitentan – Idorsia's once-daily, orally active, dual endothelin receptor antagonist – in the subgroup of African American patients enrolled in the Phase 3 PRECISION study[2] in patients with confirmed resistant hypertension. Aprocitentan, when added to a combination of at least three antihypertensive drugs (four in more than 50% of patients), produced clinically meaningful and sustained blood pressure reductions.[1] Aprocitentan also markedly decreased proteinuria in the patients with proteinuria at baseline.[1] As reported by the authors, aprocitentan was safe and well tolerated, even in those Black patients with chronic kidney disease.[1]

Hypertension is the leading modifiable cause of early mortality and cardiovascular disease worldwide, impacting an estimated 1.3 billion people globally.[3] Approximately 10% of these people have uncontrolled BP, despite receiving at least three antihypertensive medications from different classes, at optimal doses.[4,5] Compared with adults whose hypertension is well controlled, adults with uncontrolled hypertension have much greater risk of heart attack, stroke, end-stage renal disease and death.[6] Black hypertensive individuals frequently present with resistant hypertension and disproportionately increased cardiovascular risk.[7,8,9]

The endothelin (ET) pathway has been implicated in the pathogenesis of hypertension and is activated in patients prone to developing resistant hypertension,[10,11] such as Black or African American patients[12], patients with obesity[13] or obstructive sleep apnea,[14] and in comorbid conditions frequently associated with resistant hypertension such as diabetes[15,16] and chronic kidney disease.[17,18]

Prof. Keith C. Ferdinand, MD, FACC, FAHA, FASH, FNLA Professor, Tulane University School of Medicine, Tulane Heart & Vascular Institute, US, co-author of the publication and investigator in the PRECISION study, commented: "Black individuals frequently present with resistant hypertension and disproportionately increased cardiovascular risk. This is possibly related to the activated endothelin system seen in patients prone to developing resistant hypertension and this may explain why existing therapies that do not target the endothelin system have not shown optimal improvement for Black patients. Now, for the first time, we have an approved treatment targeting the endothelin system that may help fulfil an unmet need in Black patients with resistant hypertension."

The publication is accompanied by an Editorial entitled "Endothelin Antagonism: A New Era for Resistant Hypertension?"[19] from Gavin B. Chapman and Neeraj Dhaun of Edinburgh Kidney, University/BHF Centre for Cardiovascular Science, The Queen's Medical Research Institute, University

of Edinburgh, United Kingdom and Department of Renal Medicine, Royal Infirmary of Edinburgh, United Kingdom (G.B.C., N.D.).

The Editorial recognizes that the approval of aprocitentan in the US and Europe represents the first new antihypertensive to be approved in over two decades and the first via a new pathway in almost four decades. In closing, the authors conclude "Given the broad beneficial effects ET receptor antagonism has on a range of cardiovascular risk factors, it may not be long before clinicians reach for these drugs above other, more established antihypertensive medications."[19]

Prof. John M. Flack, MD, MPH, FAHA, MACP, CHS, Sergio Rabinovich Endowed Chair of Internal Medicine, Chair Departments of Medicine and Population Science and Policy, Southern Illinois University School of Medicine, Lead author of the publication and investigator in the PRECISION study, commented: "The salt-sensitive, low-renin, hypertension often seen in Black patients makes their hypertension difficult to control and increases their cardiovascular risk. In fact, Black adults with hypertension less often achieve the guideline recommended BP goals, leading to an estimated 400,000 strokes, heart attacks and other cardiovascular events that could be prevented over 10 years if blood pressure control could be achieved. In PRECISION, the effect of aprocitentan for these patients was striking and I agree with the Editorial in suggesting that we are entering a new "era" for resistant hypertension, as with aprocitentan, the dual endothelin receptor antagonist or "ERA", we can now tackle this important pathway."

Aprocitentan is approved as TRYVIO™ in the US for the treatment of systemic hypertension in combination with other antihypertensives to lower blood pressure in patients who are not adequately controlled on other drugs, and has been commercially available since October 2024.[20] Aprocitentan is approved as JERAYGO™ for the treatment of resistant hypertension in combination with other antihypertensives in the European Union[21] and the UK and marketing authorization applications are under review in Canada and Switzerland.

Notes to the editor

About Prof. Ferdinand

Keith C. Ferdinand, MD, FACC, FAHA, FASH, FNLA began his medical career with a BA in biology from the University of New Orleans. He then went on to earn an MD from Howard University College of Medicine in Washington, DC, an internship at the US Public Health Hospital in New Orleans, an internal medicine residency and cardiology fellowship at LSU Medical Center and a cardiology fellowship at Howard University Hospital, Washington, D.C. After years of doing clinical work, research and teaching at Xavier University, LSU, Baylor College of Medicine, and Emory University, Dr. Ferdinand returned to New Orleans as a Professor of Clinical Medicine at the Tulane University Heart and Vascular Institute.

Dr. Ferdinand has been heavily involved in many national organizations concerned with public health, including the Association of Black Cardiologists, of which he was the former Chair and Chief Science Officer, the American Society of Hypertension, of which he was a board member, and the Healthy Heart Community Prevention Program, a cardiovascular risk program targeting African American and other high-risk populations. He is the immediate-past Chair of the National Forum for Heart Disease and Stroke Prevention, which provides the leadership and encouragement for collaboration among over 65 organizations. Dr. Ferdinand focuses largely on cardiac risk factor evaluation and control, especially hypertension and hyperlipidemia, including communities of racial and ethnic minorities. He has had over 100 manuscripts published and has a strong media presence. His passion for patient-care is highlighted in his commitment to non-profit work and community service. In 2015 he was inducted into the Association of University Cardiologists. Prof. Ferdinand serves as a consultant to Idorsia.

About Prof. Flack

John M. Flack, M.D., M.P.H., F.A.H.A., M.A.C.P., 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 Department of Medicine at Southern Illinois University School of Medicine. He is also Chief of the Hypertension Section. 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 210 peer-reviewed manuscripts and book chapters and is an Associate Editor for the American Journal of 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 Cardiologist (ABC), the F. Dewey Dodrill Award for Excellence (2007) from the American Heart Association (AHA), the Detroit News Michiganian 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 a stint 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 is a current member of the ACP Board of Regents. Prof. Flack serves as a consultant to Idorsia.

References

1. Flack JM, et al. Aprocitentan for Blood Pressure Reduction in Black Patients. Hypertension. 2025;82:601–610.
2. Schlaich MP, et al. A randomized controlled trial of the dual endothelin antagonist aprocitentan for resistant hypertension. The Lancet, 2022; Dec 3;400(10367):1927-1937.
3. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet 2021; 398:957-80.
4. Noubiap JJ, Nansseu JR, Nyaga UF, Sime PS, Francis I, Bigna JJ. Global prevalence of resistant hypertension: a meta-analysis of data from 3·2 million patients. Heart 2019; 105: 98–105.
5. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. Eur Heart J 2018; 39: 3021–104.
6. Daugherty SL, Powers JD, Magid DJ, Tavel HM, Masoudi FA, Margolis KL, O'Connor PJ, Selby JV, Ho PM. Incidence and prognosis of resistant hypertension in hypertensive patients. Circulation. 2012 Apr 3;125(13):1635-42.
7. Ostchega Y, Fryar CD, Nwankwo T, Nguyen DT. Hypertension prevalence among adults aged 18 and over: United States, 2017–2018. NCHS Data Brief. 2020;364:1–8.
8. Flack JM, Hamaty M. Difficult-to-treat hypertensive populations: focus on African-Americans and people with type 2 diabetes. J Hypertens Suppl. 1999;17:S19–S24.
9. Egan BM, Bland VJ, Brown AL, Ferdinand KC, Hernandez GT, Jamerson KA, Johnson WR, Kountz DS, Li J, Osei K, et al. Hypertension in African Americans aged 60 to 79 years: statement from the international society of hypertension in blacks. J Clin Hypertens (Greenwich). 2015;17:252–259.
10. Dhaun N, et al. Role of endothelin-1 in clinical hypertension: 20 years on. Hypertension 2008; 52:452-9.
11. Clozel M. Aprocitentan and the endothelin system in resistant hypertension. Can J Physiol Pharmacol 2022; 100:573-83.
12. Grubbs AL, et al. Saphenous vein endothelin system expression and activity in African American patients. Arterioscler Thromb Vasc Biol 2002; 22: 1122–7.
13. Parrinello G, et al. Central obesity and hypertension: the role of plasma endothelin. Am J Hypertens 1996; 9: 1186–91.
14. Phillips BG, et al. Effects of obstructive sleep apnea on endothelin-1 and blood pressure. J Hypertens 1999; 17: 61–6.
15. Takahashi K, et al. Elevated plasma endothelin in patients with diabetes mellitus. Diabetologia 1990; 33: 306–10.
16. Solini A, et al. Resistant hypertension in patients with type 2 diabetes: clinical correlates and association with complications. J Hypertens 2014; 32: 2401–10; discussion 10.
17. Dhaun N, et al. Endothelin-1 and the kidney--beyond BP. Br J Pharmacol 2012; 167: 720–31.
18. Rossignol P, et al. The double challenge of resistant hypertension and chronic kidney disease. Lancet 2015; 386: 1588–98.
19. Chapman GB, Dhaun N. Endothelin Antagonism: A New Era for Resistant Hypertension? Hypertension. 2025;82:611–614.
20. TRYVIO (aprocitentan) Full Prescribing Information including BOXED Warning (PI and Medication Guide).
21. JERAYGO (aprocitentan) Summary of Product Characteristics (SmPC)

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).

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

The above information contains certain "forward-looking statements", relating to the company's business, which can be identified by the use of forward-looking terminology such as "estimates", "believes", "expects", "may", "are expected to", "will", "will continue", "should", "would be", "seeks", "pending" or "anticipates" or similar expressions, or by discussions of strategy, plans or intentions. Such statements include descriptions of the company's investment and research and development programs and anticipated expenditures in connection therewith, descriptions of new products expected to be introduced by the company and anticipated customer demand for such products and products in the company's existing portfolio. Such statements reflect the current views of the company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results, performance or achievements of the company to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.