



## News Release

### Media Contact:

Jennifer Silvent  
Phone: +1 973-479-9845  
[JSilvent@its.jnj.com](mailto:JSilvent@its.jnj.com)

Tina Kitt  
Phone: +41 79-219-8643  
[ckitt@its.jnj.com](mailto:ckitt@its.jnj.com)

### Investor Contact:

Raychel Kruper  
Phone: +1 732-524-6164  
[RKruper@its.jnj.com](mailto:RKruper@its.jnj.com)

## **Late-Breaking Data from Pivotal Phase 3 PRECISION Study Demonstrates Significant and Sustained Effect of Aprocitentan on Lowering Blood Pressure for Patients with Difficult-to-Control Hypertension**

*Aprocitentan is an investigational antihypertensive drug with a novel mechanism of action*

**RARITAN, NJ, November 7, 2022** – The Janssen Pharmaceutical Companies of Johnson & Johnson, in collaboration with Idorsia Ltd, today announced results from the Phase 3 PRECISION study, which found aprocitentan, an investigational, novel dual endothelin receptor antagonist (ERA), significantly reduced blood pressure (BP) and maintained the effect for up to 48 weeks when added to standardized combination background antihypertensive therapy in patients with difficult-to-control hypertension (sometimes referred to as resistant hypertension). These data were presented as a Late-Breaking Science presentation during the American Heart Association (AHA) Scientific Sessions 2022 (Session: LBS.09) and simultaneously published in [The Lancet](#).

Hypertension (HTN), or high BP (usually defined as 140/90 mmHg or above), is one of the leading causes of cardiovascular disease worldwide, impacting an estimated

1.3 billion people globally.<sup>i</sup> Approximately 10% of these people have difficult-to-control HTN, despite receiving at least three antihypertensive medications.<sup>ii,iii</sup> Research has suggested difficult-to-control HTN may be due to a lack of treatment targeting all the underlying mechanisms of the condition, in particular the endothelin (ET) pathway, which plays an important role in the development of HTN.<sup>iii,iv</sup> Compared with adults whose HTN is well controlled, adults with difficult-to-control HTN have greater risk of heart attack, stroke, end-stage renal disease (ESRD) and heart failure.<sup>v</sup>

“The challenge to achieve better BP control in patients with resistant hypertension is at least in part due to the fact that currently available treatment options leave relevant pathophysiologic mechanisms unopposed,” said Prof. Markus Schlaich, M.D., FAHA, FESC, ISHF, The University of Western Australia / Royal Perth Hospital, an investigator in the PRECISION study.<sup>1</sup> “The results of PRECISION demonstrate aprocitentan is a novel and generally well-tolerated potential treatment strategy for resistant hypertension with clinically meaningful and sustained blood pressure lowering effect.”

PRECISION evaluated the short-term and sustained effects of aprocitentan on BP lowering when added to standardized combination background antihypertensive therapy in patients with difficult-to-control HTN. A total of 730 hypertensive patients with difficult-to-control HTN were enrolled in the three-part study:

- From baseline through week 4 (part 1), the double-blind period, patients were randomized to receive aprocitentan 12.5 mg (n=243), aprocitentan 25 mg (n=243), or placebo (n=244) in a 1:1:1 ratio.
- From weeks 4-36 (part 2), the single-blind period, patients who continued to part 2 (n=704) received 25 mg aprocitentan.
- From weeks 36-48 (part 3), the double-blind withdrawal period, patients were re-randomized to receive either aprocitentan 25 mg (n=307) or placebo (n=307) in a 1:1 ratio.

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<sup>1</sup> Professor Schlaich received payment for his participation in the PRECISION study.

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.

### **Key PRECISION Findings**

The PRECISION study met its primary efficacy endpoint, which was the change in sitting systolic blood pressure (SBP), as measured by unattended automated office BP, from baseline to week 4. Specifically, after 4 weeks, aprocitentan significantly reduced SBP compared with placebo (mean change of -15.3 mmHg for aprocitentan 12.5 mg dose, -15.2 mmHg for 25 mg dose and -11.5 mmHg for placebo, for a difference versus placebo of -3.8 mmHg in the 12.5 mg group [97.5% confidence interval [CI]: -6.8, -0.8;  $p = 0.0042$ ] and -3.7 mmHg in the 25 mg group [97.5% CI: -6.7, -0.8;  $p=0.0046$ ]).

In addition to meeting its primary endpoint, the study also met its key secondary efficacy endpoint, showing sustained SBP lowering in patients receiving aprocitentan compared to placebo between week 36 and week 40. Specifically, at week 40, SBP increased with placebo compared to aprocitentan 25 mg, for a significant difference of +5.8 mmHg (95% CI: +3.7, +7.9;  $p<0.0001$ ). This difference was sustained for the final part of the study (the entire 12-week double-blind withdrawal period), up to 48 weeks.

Other key findings included:

- Similar BP lowering effects for aprocitentan were observed with ambulatory BP monitoring, which measured BP in regular intervals over a 24-hour period, at both week 4 and week 40. Specifically, the ambulatory SBP results at week 4 showed greater BP lowering effects with aprocitentan compared with placebo (12.5 mg dose: -4.2 mmHg, 95% CI: -6.2, -2.1; 25 mg dose: -5.9 mmHg, 95% CI: -7.9, -3.8). At week 40, 24-hour ambulatory SBP increased with placebo compared with aprocitentan (+6.5 mmHg; 95% CI: +4.6, +8.5).

- Treatment effect of aprocitentan was consistent across various prespecified subgroups, including sex, age, body mass index, race and geographic area.

Treatment-emergent adverse events (TEAEs) during the 4-week double-blind study period (Part 1) were reported in 28% and 37% of the patients treated with 12.5 and 25 mg aprocitentan, respectively, versus 19% in the placebo group. The most frequent adverse event with aprocitentan was mild-to-moderate fluid retention leading to discontinuation in seven patients during the study. Fluid retention 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).

“Identifying innovative approaches and novel therapies to help address some of the greatest unmet needs for patients around the world is the cornerstone of our research and development efforts. This is especially true for patients with difficult-to-control hypertension where it is critical that novel pathways are discovered to address a decades old need,” said James List, M.D., Ph.D., Global Therapeutic Area Head, Cardiovascular, Metabolism, Retina & Pulmonary Hypertension, Janssen Research & Development, LLC. “The potential addition of aprocitentan to the armamentarium holds promise for these patients.”

### **About PRECISION**

Sponsored by Idorsia, PRECISION was conducted across 193 sites in 22 countries worldwide. All eligible study participants were required to have uncontrolled BP, defined as sitting systolic BP (measured as unattended automated office BP  $\geq$ 140 mmHg), despite the use of at least three antihypertensive medications from different classes within the previous year.

During screening, all patients switched from their respective antihypertensive therapies (except beta-blockers) to standardized background therapy, including a

calcium channel blocker (amlodipine), an angiotensin receptor blocker (valsartan), and a diuretic (hydrochlorothiazide), which they received for at least four weeks before entering the second part. Patients then received placebo in addition to standardized background therapy for four additional weeks. This was followed by the active treatment period of the study, which included the three sequential parts. The safety follow-up period covered the 30 days after the last study treatment dose.

The effect on systolic and diastolic blood pressure was measured at trough by unattended automated office blood pressure (AOBP), and by 24-hour ambulatory blood pressure monitoring (ABPM) throughout the 48-week treatment period.

More information can be found on [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT03541174).

### **About aprocitentan**

Aprocitentan is an investigational, novel, oral, dual ERA, which potently inhibits the binding of ET-1 to ET<sub>A</sub> and ET<sub>B</sub> receptors. Aprocitentan has a low potential for drug-drug interaction and a mechanism of action that is intended to address the pathophysiology of difficult-to-control HTN.

### **About the Janssen/Idorsia Collaboration**

In 2017, Janssen Biotech, Inc., one of the Janssen Pharmaceutical Companies of Johnson & Johnson, entered into a collaboration agreement with Idorsia to jointly develop aprocitentan and any of its derivative compounds or products. Both parties have joint development rights over aprocitentan. Idorsia has conducted the Phase 3 development and will be responsible for the regulatory submission for the indication of the treatment of patients with difficult-to-control HTN.

### **About the Janssen Pharmaceutical Companies of Johnson & Johnson**

At Janssen, we're creating a future where disease is a thing of the past. We're the Pharmaceutical Companies of Johnson & Johnson, working tirelessly to make that future a reality for patients everywhere by fighting sickness with science, improving

access with ingenuity, and healing hopelessness with heart. We focus on areas of medicine where we can make the biggest difference: Cardiovascular, Metabolism, & Retina; Immunology; Infectious Diseases & Vaccines; Neuroscience; Oncology; and Pulmonary Hypertension.

Learn more at [www.janssen.com](http://www.janssen.com). Follow us at [@JanssenGlobal](https://twitter.com/JanssenGlobal) and [@JanssenUS](https://twitter.com/JanssenUS). Janssen Research & Development, LLC and Janssen Biotech, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson.

### **Cautions Concerning Forward-Looking Statements**

*This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of apocitinan. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Research & Development, LLC, or any of the other Janssen Pharmaceutical Companies and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 2, 2022, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q, and other filings with the Securities and Exchange Commission. Copies of these filings are available online at [www.sec.gov](http://www.sec.gov), [www.jnj.com](http://www.jnj.com) or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies nor Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments.*

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<sup>i</sup> 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.

<sup>ii</sup> 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.

<sup>iii</sup> 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.

<sup>iv</sup> Clozel M. Aprocitentan and the endothelin system in resistant hypertension. *Can J Physiol Pharmacol* 2022;100:573-83.

<sup>v</sup> 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.