Media Release
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Idorsia's JERAYGO (aprocitentan) approved in Europe as first and only ERA for the treatment of resistant hypertension

- Idorsia receives approval from the European Commission (EC) for JERAYGO™ (aprocitentan) as the first and only endothelin receptor antagonist (ERA) for the treatment of resistant hypertension.
- JERAYGO is a new oral antihypertensive therapy – the first in almost 40 years – that is working via a new therapeutic pathway.

Allschwil, Switzerland – July 1, 2024
Idorsia Ltd (SIX: IDIA) announced today that the European Commission (EC) has approved JERAYGO™ (aprocitentan) for the treatment of resistant hypertension in adult patients in combination with at least three antihypertensive medicinal products.[1] The recommended dose is 12.5 mg orally once daily. The dose can be increased to 25 mg once daily for patients tolerating the 12.5 mg dose and in need of tighter blood pressure (BP) control.[1]

Hypertension is one of the leading causes of cardiovascular disease worldwide, impacting an estimated 1.3 billion people globally.[2] Approximately 10% of these people have uncontrolled BP, despite receiving at least three antihypertensive medications from different classes, at optimal doses and they are categorized in hypertension guidelines as having resistant hypertension.[3,4]

Prof. Krzysztof Narkiewicz, MD, PhD, Head of the Department of Hypertension and Diabetology, Medical University of Gdansk, Poland, commented:
"JERAYGO is an oral antihypertensive therapy that is tackling a new therapeutic pathway – the endothelin system. JERAYGO has demonstrated clinically meaningful rapid and long-term reduction in blood pressure. What I was particularly impressed with, this effect was shown in patients with resistant hypertension, whose blood pressure remained uncontrolled despite receiving at least three antihypertensive medications as background therapy. In Europe, there are millions of patients with resistant hypertension, and they are at a higher risk of heart attack, heart failure, stroke, end-stage renal disease and death due to their high blood pressure. With JERAYGO, doctors now a have an effective new treatment option to help control blood pressure in these patients."

Alberto Gimona, MD, Head of Global Clinical Development & Medical Affairs, commented:
"We are very proud to have gained approval for JERAYGO, the first innovative anti-hypertensive drug in 40 years, acting on the endothelin pathway, which we believe is a key player in patients with resistant hypertension. We have seen a clinically meaningful and consistent blood pressure lowering across blood pressure measurement methodologies and in subgroups of patients with serious comorbidities – for example in patients with chronic kidney disease. We also saw a marked reduction in albuminuria with JERAYGO as evidenced by a decrease in baseline UACR. I'm very pleased that the wealth of data we have generated with JERAYGO is well reflected in the label. We will now work to expand marketing authorization by also applying for JERAYGO approval in the UK, Canada, and Switzerland."

André Muller, Chief Executive Officer of Idorsia commented:
"With aprocitentan, we have a largely unencumbered asset approved in the US and Europe. We continue to carefully evaluate all our funding options including potential collaborations for the commercialization of aprocitentan, while preparing to make aprocitentan available in these two key markets."

About the Phase 3 PRECISION study[1,5]
The efficacy of aprocitentan was evaluated in one randomized, double-blind (DB), placebo-controlled Phase 3 multicenter study. Patients with uncontrolled blood pressure (systolic blood pressure [SBP] ≥ 140 mmHg) despite the use of at least three antihypertensive medicinal products and following exclusion of pseudo-resistant hypertension (e.g., white coat effect, inappropriate blood pressure measurement, secondary causes of hypertension) were considered to have resistant hypertension. The patients were switched to standardized background antihypertensive therapy consisting of an angiotensin receptor blocker (valsartan 160 mg), a calcium channel blocker (amlodipine 5 or 10 mg), and a diuretic (hydrochlorothiazide 25 mg) throughout the study. Patients with concomitant use of beta-blockers continued this treatment throughout the study, in addition to the standardized background antihypertensive therapy and study treatment. A total of 730 patients received either aprocitentan 12.5 mg, aprocitentan 25 mg, or placebo once daily during the initial 4-week DB treatment (part 1). Thereafter, patients received aprocitentan 25 mg once daily during the 32-week single-blind treatment (part 2). At the end of the 32 weeks, patients were re-randomized to receive either aprocitentan 25 mg or placebo, once daily, during the 12-week double-blind withdrawal (DB-WD) treatment (part 3).

The primary efficacy endpoint was the change in sitting SBP (SiSBP) from baseline to Week 4 during DB treatment (part 1), measured at trough by unattended automated office blood pressure (uAOBP). The key secondary endpoint was the change in SiSBP measured at trough by uAOBP from DB-WD baseline (Week 36) to Week 40 (part 3).

Patients had a mean age of 61.7 years (range 24 to 84 years; 34.1% were ≥ 65 and < 75 years; 9.9% were ≥ 75 years) and 59.5% were male. Patients were White (82.9%), African American (11.2%) or Asian (5.2%). The mean body weight was 97.6 kg (range 46 to 196 kg) and mean BMI was 33.7 kg/m2 (range 18 to 64 kg/m2). Patients had a medical history of type 2 diabetes mellitus (54.1%), ischemic heart disease (30.8%), central nervous system vascular disorders (23.0%), chronic kidney disease stages 3 and 4 (22.2%; 19.3% of patients had eGFR 30-59 mL/min/1.73 m2 and 2.9% had eGFR 15-29 mL/min/1.73 m2), congestive heart failure (19.6%), and sleep apnea syndrome (14.1%). 63.0% of patients had four or more antihypertensive medicinal products.

Key PRECISION findings[1,5]
Doses of aprocitentan 12.5 and 25 mg showed a statistically significant reduction vs placebo on SiSBP at Week 4. The treatment effect was consistent for sitting diastolic blood pressure (SiDBP). The persistence of the BP-lowering effect of aprocitentan was shown in DB-WD treatment (part 3). In patients re-randomized to placebo, the mean SiSBP increased, whereas in patients re-randomized to aprocitentan 25 mg the mean effect on SiSBP was stable, resulting in a statistically significant difference. The treatment effect was consistent for SiDBP. The effect was also consistent across SBP and DBP measured by ambulatory BP monitoring (ABPM) and assessed as daytime, night-time, and 24h periods at Week 4 and Week 40. A substantial proportion (i.e., at least 90%) of the BP-lowering effect was observed within the first two weeks of treatment with aprocitentan. The effect of aprocitentan was consistent across subgroups of age (including patients ≥ 75 years), sex, race (including patients with Black or African American origin), BMI, baseline urine albumin-to-creatinine ratio (UACR), baseline eGFR and medical history of diabetes.

The most frequently reported adverse reactions with aprocitentan were edema/fluid retention (mostly peripheral edema) (9.1%, 12.5 mg; 18.4%, 25 mg) and hemoglobin decreased (3.7%, 12.5 mg; 1.2%, 25 mg). JERAYGO is contraindicated for use in women who are pregnant, breast-feeding and in women of childbearing potential who are not using reliable contraception, and patients with severe hepatic impairment.

For more information on the marketing authorization of JERAYGO in the European Union, please review the Summary of Product Characteristics (SmPC).

Notes to the editor

About aprocitentan

The team at Idorsia has been working on the research and development of endothelin receptor antagonists for more than 30 years, successfully bringing three other molecules from this class to patients in different indications. Endothelin (ET)-1, via its receptors (ET_A and ET_B), mediates a variety of effects such as vasoconstriction, fibrosis, cell proliferation, and inflammation and is upregulated in hypertension. Aprocitentan is a dual ERA that inhibits the binding of ET-1 to ET_A and ET_B receptors and hence the effects mediated by these receptors.[1]

References

1. JERAYGO™ Summary of Product Characteristics. 2024.
2. 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.
3. Noubiap JJ, et al. Global prevalence of resistant hypertension: a meta-analysis of data from 3·2 million patients. Heart 2019; 105: 98–105.
4. Williams B, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. Eur Heart J 2018; 39: 3021–104.
5. 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.

About Prof. Krzysztof Narkiewicz, MD, PhD

Professor Krzysztof Narkiewicz is the Head of the Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, Poland. His research has been focused on the role of the sympathetic nervous system and metabolic factors in regulation of cardiovascular function in physiological and pathological states, and on prevention and treatment of cardiometabolic diseases including hypertension, diabetes, coronary artery disease, congestive heart failure and obstructive sleep apnea. He has published over 700 full-text publication; (> 39 000 citations; h-index: 69). He was the President of the Scientific Council of the European Society of Hypertension (2009-2011). He was a member of the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC) preparing the 2007, 2013 and 2018 Guidelines for the Management of Arterial Hypertension. He also contributed to the 2023 ESH hypertension guidelines. Prof. Krzysztof Narkiewicz serves as a consultant to Idorsia.

About Idorsia

Idorsia Ltd is reaching out for more – We have more ideas, we see more opportunities and we want to help more patients. In order 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 is specialized in the discovery, development and commercialization of small molecules to transform the horizon of therapeutic options. Idorsia has a 25-year heritage of drug discovery, a broad portfolio of innovative drugs in the pipeline, an experienced team of professionals covering all disciplines from bench to bedside, and commercial operations in Europe and North America – the ideal constellation for bringing innovative medicines to patients.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 750 highly qualified specialists dedicated to realizing our ambitious targets.

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