



Ironwood Pharmaceuticals Initiates Phase II Clinical Trial of sGC Stimulator IW-1701 in Patients with Sickle Cell Disease

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CAMBRIDGE, Mass.--(BUSINESS WIRE)-- [Ironwood Pharmaceuticals, Inc.](#) (NASDAQ: IRWD), a commercial biotechnology company, today announced the initiation of STRONG-SCD, a Phase II clinical trial evaluating once-daily IW-1701, an orally administered soluble guanylate cyclase (sGC) stimulator, in patients with sickle cell disease.

Sickle cell disease is a debilitating genetic disorder that causes red blood cells to become sickle-shaped, reducing normal red blood cell number, blood flow and oxygen delivery to organs. Many of the symptoms of sickle cell disease are believed to be caused by a deficiency of nitric oxide (NO), an important regulator of blood flow and inflammatory processes. IW-1701 has been shown to improve NO signaling in non-clinical studies, and is being investigated for its potential to treat multiple aspects of sickle cell disease pathophysiology, including red blood cell sickling, decreased blood flow and vascular inflammation.

"There is a considerable unmet need in sickle cell disease, and patients with this condition would benefit from innovative treatments that not only prevent painful crises, organ damage and other serious complications, but also address underlying causes of these symptoms," said Christopher Wright, MD, PhD, senior vice president of global development and chief development officer at Ironwood. "By stimulating the sGC pathway, we believe IW-1701 has the potential to improve NO signaling and address the causes of both acute and chronic sickle cell disease symptoms."

STRONG-SCD is a multicenter, randomized, double-blind, placebo-controlled, dose-ranging Phase II clinical trial designed to assess the safety and tolerability of oral, once-daily IW-1701 in patients with sickle cell disease. Additional exploratory objectives include the evaluation of the pharmacokinetic profile of IW-1701 as well as its effects on sickle cell disease symptoms, health-related quality of life and biomarkers of pharmacodynamic activity. The trial is expected to enroll approximately 88 patients between 16 and 70 years of age. Patients will remain on their existing treatment regimens throughout the trial. Patients will be randomized to receive placebo or one of three dose levels of IW-1701 administered for approximately 12 weeks.

Ironwood recently presented IW-1701 data at the 2017 American Society of Hematology (ASH) Annual Meeting. In an oral presentation entitled "The Clinical-Stage sGC Stimulator IW-1701 Prevents Increase of Plasma Biomarkers of Intravascular Inflammation and Suppresses Leukocyte-Endothelial Interactions in TNF α -Treated Mice," non-clinical data were presented demonstrating that, in these models, pre-treatment with IW-1701 inhibited the intravascular inflammation typically caused by TNF α , and that the effect of IW-1701 on inflammation was enhanced when co-administered with hydroxyurea, the current standard of care for sickle cell disease. In addition, Ironwood presented data from a randomized, placebo-controlled Phase Ib multiple ascending dose study of IW-1701 tablets in healthy subjects. Data from both of these studies support the continued clinical evaluation of IW-1701 in sickle cell disease.

About Sickle Cell Disease

Sickle cell disease is an inherited red blood cell disorder that causes red blood cells to deform into a sickle shape, impacting blood flow to organs and tissues. These sickled red blood cells are more susceptible to hemolysis (rupturing). Upon red blood cell rupturing, nitric oxide (NO) is depleted due to arginase release and hemoglobin scavenging. NO is an important regulator of blood flow, and the resulting deficiency of NO is believed to contribute to disease mechanisms and symptoms of sickle cell disease.

A life-long disease, sickle cell disease affects an estimated 100,000 Americans and millions of people throughout the world. Patients with sickle cell disease can experience various complications, including attacks of severe pain called pain crises, chronic pain, acute chest syndrome, pulmonary hypertension, ankle ulcers, renal complications and an increased risk of serious infections. Severe symptoms may include strokes and pulmonary complications, which can be fatal.

About IW-1701

IW-1701, an investigational soluble guanylate cyclase (sGC) stimulator discovered and wholly-owned by Ironwood, is being studied in patients with sickle cell disease and in patients with achalasia. IW-1701 has been shown in non-clinical studies to modulate the nitric oxide/soluble guanylate cyclase/cyclic guanosine monophosphate (NO/sGC/cGMP) signaling pathway, which is believed to be implicated in achalasia and sickle cell disease. Currently in Phase II development for sickle cell disease and for achalasia, IW-1701 has the potential to address the underlying causes of these diseases by improving NO signaling and thereby increasing the second messenger cGMP.

About Ironwood's sGC Program

As a pioneering expert in cyclic GMP (cGMP), Ironwood is building on its success with linaclotide, which stimulates guanylate cyclase-C in the intestine, to develop a pipeline of soluble guanylate cyclase (sGC) stimulators. sGC plays an important role in regulating diverse physiological processes; dysregulation of sGC may play a role in multiple serious diseases. Ironwood's sGC stimulators are believed to harness the nitric oxide (NO)/sGC/cGMP pathway by working synergistically with NO to improve blood flow and metabolism and decrease inflammation and fibrosis.

Ironwood is advancing IW-1973, its lead sGC stimulator, for the potential treatment of diabetic nephropathy and of heart failure with preserved ejection fraction (HFpEF). Ironwood's second clinical sGC stimulator, IW-1701, is being developed for the potential treatment of achalasia and of sickle cell disease. In addition, Ironwood has a pipeline of other sGC stimulators in pre-clinical development.

About Ironwood Pharmaceuticals

Ironwood Pharmaceuticals (NASDAQ: IRWD) is a commercial biotechnology company focused on creating medicines that make a difference for patients, building value for our fellow shareholders, and empowering our passionate team. We are commercializing two innovative primary care products: linaclotide, the U.S. branded prescription market leader for adults with irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC), and lesinurad, which is approved to be taken with a xanthine oxidase inhibitor (XOI), or as a fixed-dose combination with allopurinol, for the treatment of hyperuricemia associated with gout. We are also advancing a pipeline of innovative product candidates in areas of significant unmet need, including uncontrolled gastroesophageal reflux disease, diabetic nephropathy, heart failure with preserved ejection fraction, achalasia and sickle cell disease. Ironwood was founded in 1998 and is headquartered in Cambridge, Mass. For more information, please visit www.ironwoodpharma.com or www.twitter.com/ironwoodpharma; information that may be important to investors will be routinely posted in both these locations.

This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including statements about Ironwood's sGC program and the clinical program for IW-1701, including the design, size, scope and potential results of the Phase II clinical trial; the mechanism of action of IW-1701; the size of the potential patient population; the data to be generated from the Phase II clinical trial; the timing that these data are expected to be available; the cause of the disease and the symptoms suffered by the potential patient population; and IW-1701 as a potential treatment for sickle cell disease. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include those related to the risk that we are unable to enroll as many patients in the clinical study or complete the Phase II clinical trial on the same timeline as we currently anticipate; the risk that the data from the clinical trial may not be available when we currently anticipate them or do not demonstrate the results we expect, including with respect to efficacy, safety and tolerability; the risk that the Phase II clinical trial needs to be discontinued for any reason, including safety, enrollment, manufacturing or economic reasons; the patient population is not as large as we presently estimate; the effectiveness of development and commercialization efforts by us and our partners; preclinical and clinical development, manufacturing and formulation development; the risk that findings from our completed nonclinical and clinical studies may not be replicated in later studies; decisions by regulatory authorities; the risk that we may never get sufficient patent protection for IW-1701 or that we are not able to successfully protect such patents; the outcomes in legal proceedings to protect or enforce the patents relating to IW-1701; developments in the intellectual property landscape; challenges from and rights of competitors or potential competitors; the risk that our planned investments do not have the anticipated effect on our business or the IW-1701 program; and those risks listed under the heading "Risk Factors" and elsewhere in Ironwood's Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, and in our subsequent SEC filings. These forward-looking statements (except as otherwise noted) speak only as of the date of this press release, and Ironwood undertakes no obligation to update these forward-looking statements.

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