Ironwood Pharmaceuticals Announces FDA Orphan Drug Designation for Olinciguat for the Treatment of Sickle Cell Disease

June 7, 2018

– Olinciguat Phase II trial in sickle cell disease continues to enroll patients –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 7, 2018-- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD), a commercial biotech company, today announced that the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation to olinciguat (IW-1701) for the treatment of patients with sickle cell disease. Olinciguat is an orally administered soluble guanylate cyclase (sGC) stimulator.

"There is an urgent need for new, innovative treatments for patients with sickle cell disease, a debilitating and potentially fatal inherited blood disorder that causes painful crises, organ damage and other serious complications," said Christopher Wright, M.D., Ph.D., senior vice president of global development and chief development officer. "The orphan drug designation adds momentum to our clinical program investigating olinciguat, which has the potential to improve multiple aspects of sickle cell disease pathophysiology. The designation is also an important milestone in Ironwood's evolution as we advance our pipeline of sGC stimulators focused on the treatment of serious and orphan diseases."

The FDA's Office of Orphan Drug Products grants orphan status to drugs intended to treat rare disorders that affect fewer than 200,000 people in the U.S. The designation provides certain benefits to the drug developer, including seven years of market exclusivity upon FDA approval, prescription drug user fee waivers and tax credits for qualified clinical trials.[1,2]

Ironwood is currently enrolling patients in STRONG-SCD, a multicenter, randomized, double-blind, placebo-controlled, dose-ranging Phase II trial evaluating olinciguat for the potential treatment of sickle cell disease. Ironwood expects to enroll approximately 80 patients into the Phase II trial, which is designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of olinciguat in patients with sickle cell disease. Further details about the trial can be found at clinicaltrials.gov using the identifier number NCT03285178.

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 Olinciguat

Olinciguat (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. Olinciguat 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, olinciguat 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 praliciguat (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, olinciguat (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 persistent 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.

Forward-Looking Statements

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 olinciguat, including the design, size, scope and potential results of the Phase II clinical trial; the mechanism of action of olinciguat; the size of the potential patient population; the data to be generated from the Phase II clinical trial; the cause of the disease and the symptoms suffered by the potential patient population; and olinciguat 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 olinciguat or that we are not able to successfully protect such patents; the outcomes in legal proceedings to protect or enforce the patents relating to olinciguat; 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 olinciguat 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 March 31, 2018, 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.

[1] "Designating an Orphan Product: Drugs and Biological Products." US Food and Drug Administration. https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/HowtoapplyforOrphanProductDesignation/default.htm. Published February 16, 2018. Accessed June 6, 2018.

[2] "FDA at Rare Disease Day / February 28, 2011." US Food and Drug Administration. https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/ucm239698.htm. Published November 3, 2017. Accessed June 6, 2018.

View source version on businesswire.com: https://www.businesswire.com/news/home/20180607006163/en/

Source: Ironwood Pharmaceuticals, Inc.

Ironwood Pharmaceuticals, Inc.
Meredith Kaya, 617-374-5082
Vice President, Investor Relations and Corporate Communications
mkaya@ironwoodpharma.com