October 25, 2016

Ironwood Highlights Breadth of Gout Research with Presentations at the American College of Rheumatology 2016 Annual Meeting

-Includes highlights of safety and efficacy data for ZURAMPIC® (lesinurad) from extension studies-

-Additional presentations elucidate the potential long-term health consequences of gout-

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) today announced a series of oral and poster presentations to be presented at the upcoming American College of Rheumatology (ACR) Annual Meeting in Washington, D.C. from November 11 to 16, 2016.

The poster presentations include data from two lesinurad extension studies that enrolled patients from the pivotal Phase III CLEAR1, CLEAR2 and CRYSTAL trials, as well as a pooled analysis of renal safety from pivotal Phase III and extension studies of lesinurad, and an integrated safety study of lesinurad's three pivotal trials and extension studies. Results from the CLEAR1 pivotal trial were published in the August 2016 issue of *Arthritis & Rheumatology.*

Other presentations will address the potential long-term health consequences of gout with respect to such topics as heart failure, cardiometabolic risk, and progression of chronic kidney disease.

The titles and scheduled times of the presentations are as follows:

Safety and Efficacy of Lesinurad:
Examination of Serum Uric Acid (sUA) Lowering and Safety With Extended Lesinurad + Allopurinol Treatment in Subjects With Gout (CLEAR Extension) (abstract #208, poster), to be presented during the Metabolic and Crystal Arthropathies Poster Session I: Clinical Practice on Sunday, Nov. 13, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Kenneth G. Saag, M.D., M.Sc., University of Alabama at Birmingham.

Clinical Response of Tophus and Flares to Extended Use of Lesinurad in Combination With a Xanthine Oxidase Inhibitor in Patients With Gout (*CLEAR/CRYSTAL Extension)* (abstract #209, poster), to be presented during the Metabolic and Crystal Arthropathies Poster Session I: Clinical Practice on Sunday, Nov. 13, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Thomas Bardin, M.D., Lariboisière Hospital, Paris, France.

Renal Safety of Lesinurad: A Pooled Analysis of Phase III and Extension Studies (abstract #206, poster), to be presented during the Metabolic and Crystal Arthropathies Poster Session I: Clinical Practice on Sunday, Nov. 13, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Robert Terkeltaub, M.D., University of California, San Diego.

Integrated Safety of Lesinurad, A Novel Uric Acid Reabsorption Inhibitor for the Treatment of Gout (abstract #207, poster), to be presented during the Metabolic and Crystal Arthropathies Poster Session I: Clinical Practice on Sunday, Nov. 13, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Michael A. Becker, M.D., University of Chicago.

Potential Long-Term Health Consequences of Gout:
Rate of Hospitalization for Heart Failure Is Lower in Patients with Controlled Gout Versus Uncontrolled Gout (abstract #1242, poster), to be presented during the Health Services Research Poster Session II on Monday, Nov. 14, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Robert Morlock, Ph.D., Your Care Choice, Ann Arbor, MI.

Cardiometabolic Risk and Subclinical Urate Deposits in Patients with Symptomatic Hyperuricemia and Metabolic Syndrome (abstract #2293, poster), to be presented during the Innate Immunity and Rheumatic Disease Poster Session II: Epidemiology and Mechanisms of Disease on Tuesday, Nov. 15, 2016, 9:00 a.m.-11:00 a.m. Eastern Time, by Seoyoung C. Kim, M.D., Sc.D., MSCE, Brigham and Women's Hospital and Harvard Medical School.

Association of Gout with Risk of Advanced Chronic Kidney Disease (abstract #3188, oral), to be presented during the Epidemiology and Public Health Oral Session III: Psoriatic Arthritis and More on Wednesday, Nov. 16, 2016, 11:00 a.m. - 12:30 p.m. Eastern Time, by Austin Stack, M.D., M.Sc., FRCPI, University Hospital Limerick & Health Research Institute,

University of Limerick, Limerick, Ireland.

Disease State and Mechanism of Action Studies:
Presence of Monosodium Urate Crystals by Dual-Energy Computed Tomography in Gout Patients Treated with Allopurinol (abstract #219, poster), to be presented during the Metabolic and Crystal Arthropathies Poster Session I: Clinical Practice on Sunday, Nov. 13, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Nicola Dalbeth, MBChB, M.D., FRACP, University of Auckland, Auckland, New Zealand.

Evidence of Phospho-Degron Regulating Expression of Urate Secretory Transporter ABCG2 (abstract #2274, poster), to be presented during the Metabolic and Crystal Arthropathies Poster Session II: Epidemiology and Mechanisms of Disease on Tuesday, Nov. 15, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Alexis Hofherr, M.D., Ph.D., University of Freiburg Medical Center, Freiburg im Breisgau, Germany.

Fructose Amplifies Inflammatory Potential in Human Monocytic Cells Via Reduction of AMP-Activated Protein Kinase Activity (abstract #2268, poster), to be presented during the Innate Immunity and Rheumatic Disease Poster Session II on Tuesday, Nov. 15, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Xihua Cao, Ph.D., Veterans Medical Research Foundation (VMRF), San Diego, California.

Health Economics Studies:
Accuracy of HumaSens-plus Point-of-Care Uric Acid Meter Using Capillary Blood Obtained by Fingertip Puncture (abstract #218, poster), to be presented during the Metabolic and Crystal Arthropathies Poster Session I: Clinical Practice on Sunday, Nov. 13, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Stephanie Fabre, M.D., M.Sc., Lariboisière Hospital, Paris, France.

*Comparing the Burden of Illness of Patients with Tophaceous and Non-Tophaceous Gout in France, Germany, Italy, Spain, UK, and USA (*abstract #226, poster), to be presented during the Metabolic and Crystal Arthropathies Poster Session I:

Clinical Practice on Sunday, Nov. 13, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Puja Khanna, M.D., M.P.H., University of Michigan.

Relationship Between Patient and Disease Factors and Severity of Gout in a Real-World Population (abstract #229, poster), to be presented during the Metabolic and Crystal Arthropathies Poster Session I: Clinical Practice on Sunday, Nov. 13, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Michael Pillinger, M.D., New York University.

Health Economics of Uncontrolled Gout in the United States: A Systematic Literature Review (abstract #2241, poster), to be presented during the Health Services Research - Poster Session III on Tuesday, Nov. 15, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Shaum Kabadi, Ph.D., M.P.H., AstraZeneca.

Development and Pilot Testing of an Online Educational Tool for Gout Patients — Mygoutcare® (abstract #3130, oral), to be presented during the Metabolic and Crystal Arthropathies Oral Session II: Clinical Practice on Wednesday, Nov. 16, 2016, 9:00 a.m. - 10:30 a.m. Eastern Time, by Puja Khanna, M.D., M.P.H., University of Michigan.

*Serum Uric Acid Testing Practices Over Five Years Among Incident Gout Cases (*abstract #1225, poster), to be presented during the Health Services Research - Poster Session II on Monday, Nov. 14, 2016, 9:00 a.m. - 11:00 a.m. Eastern Time, by Dena Jaffe, Ph.D., Kantar Health, Tel Aviv, Israel.

About Hyperuricemia and Gout
Gout is a highly symptomatic and painful form of inflammatory arthritis affecting an estimated eight million people in the U.S. It is caused by an underlying metabolic disorder, hyperuricemia - high levels of uric acid in the blood - and can lead to painful flares, characterized by excruciating pain, inflammation, swelling and tenderness in one or more joints. Gout is commonly hereditary and not only a lifestyle disease. While diet and lifestyle changes are important in managing gout and its comorbidities, they are often not enough to get patient serum uric acid (sUA) levels to target.

Approximately four million patients are treated with a xanthine oxidase inhibitor (XOI), either allopurinol or febuxostat, for gout in the U.S. Of these, an estimated two million patients are uncontrolled and are not achieving target serum uric acid (sUA) levels < 6 mg/dL as recommended by the American College of Rheumatology, despite treatment with an XOI alone. These patients continue to suffer from flares despite treatment with an XOI alone, and may face serious long-term consequences that can result from having uncontrolled sUA levels.

About ZURAMPIC® (lesinurad) 200 mg tablets
ZURAMPIC® (lesinurad) is a URAT1 inhibitor approved by the FDA for use in combination with a xanthine oxidase inhibitor (XOI) for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels (sUA) with an XOI alone. ZURAMPIC is not recommended for the treatment of asymptomatic hyperuricemia and should not be used as a monotherapy. XOIs reduce the production of uric acid; ZURAMPIC increases renal excretion of uric acid by

selectively inhibiting the action of URAT1, the UA transporter responsible for the majority of renal UA reabsorption. The dual-mechanism combination of ZURAMPIC plus an XOI (allopurinol or febuxostat) can address both inefficient excretion and overproduction of UA, thereby lowering sUA levels. The safety and efficacy of ZURAMPIC were established in three Phase III clinical trials that evaluated a once-daily dose of ZURAMPIC in combination with the XOI allopurinol or febuxostat compared to XOI alone. Visit www.zurampic.com for more information about ZURAMPIC.

Important Safety Information

WARNING: RISK OF ACUTE RENAL FAILURE MORE COMMON WHEN USED WITHOUT A XANTHINE OXIDASE INHIBITOR (XOI)
-- Acute renal failure has occurred with ZURAMPIC and was more common when ZURAMPIC was given alone
-- ZURAMPIC should be used in combination with an XOI

Contraindications:

- Severe renal impairment (eCLcr less than 30 mL/min), end-stage renal disease, kidney transplant recipients, or patients on dialysis
- Tumor lysis syndrome or Lesch-Nyhan syndrome

Warnings and Precautions:

- **Renal events:** Adverse reactions related to renal function have occurred after initiating ZURAMPIC. A higher incidence was observed at the 400-mg dose, with the highest incidence occurring with monotherapy use. Monitor renal function at initiation and during therapy with ZURAMPIC, particularly in patients with eCLcr below 60 mL/min or with serum creatinine elevations 1.5 to 2 times the pre-treatment value, and evaluate for signs and symptoms of acute uric acid nephropathy. Interrupt treatment with ZURAMPIC if serum creatinine is elevated to greater than 2 times the pre-treatment value or if there are symptoms that may indicate acute uric acid nephropathy. ZURAMPIC should not be restarted without another explanation for the serum creatinine abnormalities. ZURAMPIC should not be initiated in patients with an eCLcr less than 45 mL/min.
- **Cardiovascular events:** In clinical trials, major adverse cardiovascular events (defined as cardiovascular deaths, non-fatal myocardial infarctions, or non-fatal strokes) were observed with ZURAMPIC. A causal relationship has not been established.

Adverse Reactions:

- Most common adverse reactions with ZURAMPIC (in combination with an XOI and more frequently than on an XOI alone) were headache, influenza, blood creatinine increased, and gastroesophageal reflux disease

Indication and Limitations of Use for ZURAMPIC:
ZURAMPIC is a URAT1 inhibitor indicated in combination with an XOI for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with an XOI alone.

- ZURAMPIC is not recommended for the treatment of asymptomatic hyperuricemia
- ZURAMPIC should not be used as monotherapy

Please see full Prescribing Information, including Boxed WARNING,
http://www.azpicentral.com/zurampic/zurampic.pdf.

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 advancing a pipeline of innovative medicines in areas of significant unmet need, including irritable bowel syndrome with constipation (IBS-C)/chronic idiopathic constipation (CIC), uncontrolled gout, refractory gastroesophageal reflux disease, and vascular and fibrotic diseases. We discovered, developed and are commercializing linaclotide, the U.S. branded prescription market leader in the IBS-C/CIC category, and we are applying our proven R&D and commercial capabilities to advance multiple internally-developed and externally-accessed product opportunities. 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.

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