April 26, 2016

Ironwood Pharmaceuticals Enters into U.S. Licensing Agreement with AstraZeneca for Lesinurad

- Includes FDA-approved ZURAMPIC® (lesinurad), expected to launch second half 2016 for hyperuricemia associated with uncontrolled gout, and lesinurad/allupironol fixed-dose combination -

- Leverages Ironwood's proven commercial capabilities in symptomatic diseases with high unmet need; Ironwood expects at least five U.S. launches by 2020 across its portfolio -

- $100M up front paid with cash on hand; Ironwood expects < $70M cash use for operations in 2016 and cash flow positive during 2018 -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ:IRWD) announced today that it has entered into a licensing agreement with AstraZeneca plc for the exclusive U.S. rights to lesinurad. Lesinurad 200mg tablets were approved as ZURAMPIC® by the U.S. Food and Drug Administration (FDA) in December 2015 for use in combination with a xanthine oxidase inhibitor (XOI) for the treatment of hyperuricemia associated with uncontrolled gout.

Gout is a serious, progressive and debilitating form of inflammatory arthritis. As many as two million patients in the U.S. on urate-lowering therapy remain inadequately controlled, as XOI treatment alone is not sufficient to achieve their treatment goals. ZURAMPIC is not recommended for the treatment of asymptomatic hyperuricemia and should not be used as monotherapy.

Under the terms of the agreement, Ironwood will make an up-front payment to AstraZeneca of $100 million to acquire exclusive U.S. rights to all products containing lesinurad, including the fixed-dose combination of lesinurad and allopurinol. AstraZeneca plans to submit the fixed-dose combination program for FDA regulatory review in the second half of 2016. Ironwood will pay AstraZeneca tiered single-digit royalties on product sales as well as sales-related and other milestones of up to $165 million. AstraZeneca will manufacture and supply ZURAMPIC, provide certain product support services to Ironwood and complete the FDA post-approval commitment on Ironwood's behalf.

"This transaction enables Ironwood to leverage our strong commercial capabilities to advance a durable franchise of innovative medicines addressing a significant unmet need in which patients are highly motivated and seeking relief - this is precisely the kind of opportunity the Ironwood team is successfully executing on in IBS-C and CIC," said Tom McCourt, Chief Commercial Officer of Ironwood. "With focused investment into the gout franchise over time, we believe we can maximize cash flows and accelerate our progress as a top-performing commercial biotechnology company: following this transaction, we expect to execute on at least five new launches in the U.S. by 2020, beginning with ZURAMPIC in the second half of 2016 and continuing with, if approved, 72 mcg linaclotide in 2017 and a lesinurad-allopurinol fixed-dose combination in 2018."

Luke Miels, Executive Vice President, Global Product and Portfolio Strategy, AstraZeneca, said, "We're pleased to be entering into this agreement with Ironwood, a company with whom we already have a number of successful commercial partnerships. Our new agreement with Ironwood will ensure the successful launch of ZURAMPIC in the U.S., while allowing us to concentrate our resources on the innovative medicines in our main therapy areas."

The development of AstraZeneca's gout portfolio is led by Ardea Biosciences, a wholly-owned subsidiary. The transaction does not include the transfer of any AstraZeneca or Ardea employees or facilities. AstraZeneca also retains ownership of the rest of the Ardea portfolio, including RDEA3170, a Phase IIb-ready, potent, selective uric acid reabsorption inhibitor. Under the terms of the agreement, Ironwood will have certain rights to potentially access RDEA3170 in gout indications in the U.S. The licensing agreement is expected to close in the second quarter of 2016, subject to antitrust approval in the U.S.

Ironwood Financial Considerations

Ironwood expects to pay the $100 million up-front fee from cash on hand and does not anticipate requiring any financing to complete the transaction. Ironwood is updating its 2016 cash flow guidance: the company now expects to use less than $70

million in cash for operations in 2016, up from less than $60 million as previously guided, to incorporate ZURAMPIC integration and launch investments. Ironwood expects to provide updated guidance regarding total operating expenses for 2016 during its second quarter 2016 investor update. Initially, Ironwood expects less than $75 million in annual incremental commercial expenses associated with the gout franchise, with focused investment over time to maximize cash flow. The transaction is not expected to affect 2016 LINZESS marketing and sales expenses.

Ironwood expects the transaction to be cash flow accretive in 2019 and beyond and to add significant revenue, with annual U.S. sales estimated to exceed $300 million at peak and commercial margins expected to exceed 60% by 2022. ZURAMPIC and the lesinurad-allopurinol fixed-dose combination product have patent protection into at least 2028. Additionally, Ironwood expects to become cash flow positive during 2018 and believes that the growing contribution from its commercial business and cash on hand are sufficient to fully fund its core business inclusive of the gout franchise without the need to raise additional capital.

Webcast Information: Conference Call Today at 8:00 a.m. ET

Ironwood will host a conference call and webcast at 8:00 a.m. Eastern Time on Tuesday, April 26, 2016. Individuals interested in participating in the call should dial (877) 643-7155 (U.S. and Canada) or (914) 495-8552 (international) using conference ID number 98937375. To access the webcast, please visit the Investors section of Ironwood's website at www.ironwoodpharma.com at least 15 minutes prior to the start of the call to ensure adequate time for any software downloads that may be required.

The call will be available for replay via telephone starting April 26, 2016, at approximately 11:00 a.m. Eastern Time, running through 11:00 a.m. Eastern Time on May 3, 2016. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 98937375. The archived webcast will be available on Ironwood's website for 14 days beginning approximately one hour after the call has completed.

About ZURAMPIC® (lesinurad) 200mg tablets

ZURAMPIC® (lesinurad) is the first Selective Uric Acid Reabsorption Inhibitor (SURI); it works selectively to complement xanthine oxidase inhibitors (XOIs) in the treatment of hyperuricemia associated with uncontrolled gout. ZURAMPIC is not recommended for the treatment of asymptomatic hyperuricemia and should not be used as monotherapy. XOIs reduce the production of uric acid; ZURAMPIC increases the excretion of uric acid. Together, the combination of ZURAMPIC and an XOI provides a dual mechanism of action that both decreases production and increases excretion of uric acid, thereby lowering serum uric acid (sUA) levels in patients who have not achieved target serum uric acid levels with XOI treatment alone. ZURAMPIC selectively inhibits the function of transporter proteins urate transporter (URAT1) and organic anion transporter 4 (OAT4), involved in uric acid reabsorption in the kidney. In humans, it does not inhibit OAT1 and OAT3, which are drug transporters in the kidney associated with drug-drug interactions. The safety and efficacy of ZURAMPIC was 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.

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, and evaluate for signs and symptoms of acute uric acid nephropathy. ZURAMPIC should not be initiated in patients with an eCLcr less than 45 mL/min

- **Cardiovascular events:** Major adverse cardiovascular events 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, at: http://www.azpicentral.com/zurampic/zurampic.pdf.

About Hyperuricemia and Gout

Gout is a serious, progressive and debilitating form of inflammatory arthritis that affects more than 8 million people in the U.S., with approximately 4 million of those patients on treatment, creating a market estimated at $1 billion. Approximately 2 million gout patients suffer from uncontrolled gout, in which traditional first-line xanthine oxidase inhibitor (XOI) treatment alone is not sufficient to achieve target serum uric acid (sUA) levels. Among patients treated in clinical trials, less than 50% of patients on the XOI allopurinol 300mg reached sUA target levels < 6.0mg/dL.

The underlying cause of gout is hyperuricemia (elevated sUA), which leads to the deposition of crystals primarily in the joints and also in other tissues. This can result in recurrent attacks of inflammatory arthritis and, if left uncontrolled, could lead to chronic, progressive arthritis and tophus (visible deposits of urate crystals) formation. The goal of sUA lowering treatment is to reduce sUA levels to the target level of < 6.0mg/dL as recommended by both the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR). For patients who cannot reach this target on an XOI alone, the current ACR and EULAR guidelines recommend adding an agent that increases uric acid excretion.

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 an innovative pipeline of medicines in multiple areas of significant unmet need, including irritable bowel syndrome with constipation (IBS-C)/chronic idiopathic constipation (CIC), vascular and fibrotic diseases, and refractory gastroesophageal reflux disease, among others. 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.

About AstraZeneca

AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three main therapy areas - respiratory, inflammation, autoimmune disease (RIA), cardiovascular and metabolic disease (CVMD) and oncology - as well as in infection and neuroscience. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit: www.astrazeneca.com

This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including, but not limited to, statements about the benefits anticipated from the addition of the gout franchise to Ironwood's portfolio; the timing of the closing of the lesinurad transaction; development, launch and

commercialization plans for lesinurad and our product candidates; market size, growth and opportunity, including peak sales, and potential demand for lesinurad, as well as its potential impact on applicable markets; the potential indications for, and benefits of, lesinurad; the anticipated timing of regulatory developments for the fixed-dose combination of lesinurad and allopurinol; the design, timing and results of clinical and preclinical studies; the timing of filings with regulatory authorities; expected periods of patent exclusivity; and our company's financial performance and results, and guidance and expectations related thereto, including our projected cash needs and expectations regarding the need for future financings, expectations regarding the accretive nature of the transaction and the timing of such accretion, revenue from the transaction, commercial margin, cash flows, operating expenses, commercial expenses, the effect of the transaction on 2016 LINZESS marketing and sales expense, and the timing of providing updated guidance on total operating expenses following closing. 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, but are not limited to, the risk that the transaction does not close or is delayed; the risk that we are unable to successfully integrate lesinurad into our existing business or are unable to realize the anticipated benefits of the lesinurad transaction; those related to our growth strategy; decisions made by U.S. regulatory authorities, the U.S. Patent and Trademark Office and their foreign counterparts; intellectual property rights of competitors or potential competitors; efficacy, safety and tolerability of lesinuard, linaclotide and our product candidates; competition in disease states; the commercial potential of lesinurad, linaclotide, our product candidates and the other products that we promote; and the risk that we are unable to manage our operating expenses and capital expenditures due to foreseeable or unforeseeable events or occurrences. Applicable risks also include those that are listed under the heading "Risk Factors" and elsewhere in Ironwood's Annual Report on Form 10-K for the year ended December 31, 2015 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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