November 2, 2017

Ironwood Pharmaceuticals Provides Third Quarter 2017 Investor Update

- Ironwood revenue grew 31% to $87 million in 3Q 2017 over 3Q 2016 -

- LINZESS® (linaclotide) U.S. net sales increased 16% to $191 million and net profit increased 36% to $111 million in 3Q 2017 over 3Q 2016 -

- Launched DUZALLO® (lesinurad and allopurinol), a once-daily fixed-dose combination treatment for patients with uncontrolled gout -

- Advanced innovative development candidates with positive IW-3718 Phase IIb trial results and initiation of IW-1973 Phase II trials in diabetic nephropathy and HFpEF -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ:IRWD), a commercial biotechnology company, today provided an update on its third quarter 2017 results and recent business activities.

"Ironwood's strong performance during the third quarter was driven by continued growth in LINZESS demand and brand profitability, growing contribution from our linaclotide partnership in Japan, the DUZALLO launch, and the advancement of our innovative development candidates," said Peter Hecht, chief executive officer at Ironwood. "Looking ahead, we expect strong revenue growth, expanding commercial contribution and financial discipline to propel us to positive cash flow during 2018. We continue to invest prudently in R&D, and believe our development candidates have the potential to deliver medicines addressing serious unmet medical needs, accelerate growth and generate outstanding value to both patients and shareholders."

Third Quarter 2017 and Recent Highlights

Irritable Bowel Syndrome with Constipation (IBS-C) / Chronic Idiopathic Constipation (CIC)

- *LINZESS.* U.S. net sales, as reported by Ironwood's U.S. collaboration partner Allergan plc, were $190.9 million in the third quarter of 2017, a 16% increase compared to the third quarter of 2016. Ironwood and Allergan share equally in brand collaboration profits.
  - Total LINZESS prescription volume in the third quarter of 2017 included over 29 million LINZESS capsules, an 18% increase in capsules compared to the third quarter of 2016, per QuintilesIMS.
  - More than 780,000 total LINZESS prescriptions were filled in the third quarter of 2017, a 13% increase compared to the third quarter of 2016, per QuintilesIMS.
  - Since the launch of LINZESS in December 2012, greater than 1.5 million unique patients have filled more than 9 million prescriptions, per QuintilesIMS.
  - Net profit for the LINZESS U.S. brand collaboration, including commercial and research and development (R&D) expenses, was $111.0 million in the third quarter of 2017, a 36% increase compared to the third quarter of 2016.
    - LINZESS commercial margin was 66% in the third quarter of 2017 compared to 61% in the third quarter 2016.
- *Linaclotide Delayed Release*. During the third quarter, Ironwood and Allergan optimized the linaclotide life cycle strategy to more effectively and efficiently support the achievement of the program's key objectives, which include: (1) strengthening the clinical profile of linaclotide by obtaining additional abdominal symptom claims including bloating and discomfort, two highly bothersome symptoms associated with IBS-C, and (2) expanding the clinical utility of linaclotide by demonstrating the pain-relieving effect of a delayed release formulation of linaclotide in all IBS subtypes. Specifically, the companies:
  - identified a shortened development path intended to obtain additional abdominal symptom claims through a single Phase III trial with LINZESS expected to begin in 2018; and

- plan to advance linaclotide delayed release-2 (DR2) as a visceral, non-opioid, pain-relieving agent for patients suffering from all subtypes of IBS, including IBS-C, IBS-mixed and IBS with diarrhea.
- The companies no longer intend to pursue linaclotide delayed release-1.

Uncontrolled Gout

- *DUZALLO.* In August 2017, DUZALLO was approved by the U.S. Food and Drug Administration (FDA) for the treatment of hyperuricemia in patients who have not achieved target serum uric acid levels with a medically appropriate dose of allopurinol alone. DUZALLO became commercially available in October 2017 and is the first FDA-approved fixed-dose combination treatment that addresses both causes of hyperuricemia in gout, over-production and under-excretion of serum uric acid, in a single pill.
  - Ironwood paid AstraZeneca a $15.0 million milestone upon the approval of DUZALLO during the third quarter of 2017.
- *ZURAMPIC® (lesinurad).* In October 2016, Ironwood began commercializing ZURAMPIC in the U.S. for the treatment of hyperuricemia in patients with uncontrolled gout who are already taking a xanthine oxidase inhibitor (XOI), such as allopurinol or Uloric® (febuxostat).
  - ZURAMPIC U.S. net sales were $0.7 million in the third quarter of 2017.
  - 2,066 total ZURAMPIC prescriptions were filled in the third quarter of 2017, per QuintilesIMS.

Uncontrolled Gastroesophageal Reflux Disease (GERD)

- IW-3718 is being developed for the potential treatment of uncontrolled GERD.
  - In July 2017, Ironwood announced positive top-line data from a Phase IIb clinical trial of IW-3718 in adult patients with uncontrolled GERD. Data from the trial indicated that twice-daily, oral dosing of IW-3718 1500 mg plus a proton pump inhibitor (PPI) significantly reduced heartburn severity in patients with uncontrolled GERD compared to patients treated with a PPI alone, and that more than half of these IW-3718-treated patients were responders with a clinically meaningful reduction in heartburn severity. IW-3718 1500 mg was well tolerated in the trial. The most commonly reported adverse event overall was constipation.
  - Ironwood has made important progress towards initiating Phase III trials with IW-3718 1500 mg. Ironwood continues to expect the trials to begin in the second half of 2018, pending end of Phase II meetings with the FDA.

Diabetic Nephropathy and Heart Failure with Preserved Ejection Fraction (HFpEF)

- IW-1973, Ironwood's lead investigational soluble guanylate cyclase (sGC) stimulator, is being developed for the potential treatment of diabetic nephropathy and HFpEF. Both diseases affect millions of patients around the world, including an estimated eight million Americans suffering from diabetic nephropathy and an estimated three million Americans suffering from HFpEF. Diabetic nephropathy is the leading cause of end-stage renal disease. There are few treatment options available to markedly delay the steady decline of renal function leading to dialysis or kidney transplant. HFpEF is a highly symptomatic condition with high rates of morbidity and mortality, and no approved treatments available. Ironwood initiated Phase II clinical trials with IW-1973 in diabetic nephropathy and in HFpEF.
  - *Diabetic nephropathy.* A randomized, double-blind, placebo-controlled, dose-ranging Phase II trial designed to evaluate the safety and efficacy of IW-1973 in patients with diabetic nephropathy. The trial is expected to enroll approximately 150 patients. The primary endpoint is seeking to assess the urinary albumin-to-creatinine ratio, an indicator of kidney function in diabetic nephropathy.
  - *HFpEF.* A randomized, double-blind, placebo-controlled, dose-ranging Phase II trial designed to evaluate the safety and efficacy of IW-1973 in patients with HFpEF. The trial is expected to enroll approximately 325 patients. The primary endpoint is seeking to assess the effect of IW-1973 on peak exercise capacity.
  - Ironwood no longer intends to pursue IW-1973 in resistant hypertension.
- Data from two Phase IIa studies with IW-1973 in diabetic patients with hypertension are expected by the end of 2017.

Sickle Cell Disease and Achalasia

- IW-1701, Ironwood's second clinical sGC stimulator, is being developed for the potential treatment of achalasia and sickle cell disease.
  - *Achalasia.* Ironwood continues to enroll patients with achalasia in a randomized, double-blind, placebo-controlled, single-dose Phase IIa study of IW-1701. This study is designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of IW-1701 in this patient population. Due to slower than expected

enrollment, data from this study are now expected in 2018.

- *Sickle Cell Disease.* Ironwood expects to initiate a randomized, double-blind, placebo-controlled, dose-ranging Phase II trial of IW-1701 in patients with stable sickle cell disease by the end of 2017. The Phase II trial is expected to enroll approximately 80 patients and is designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of IW-1701 in these patients.

Global Collaborations and Partnerships

- Ironwood's partner, Astellas Pharma Inc., is commercializing LINZESS for adults with IBS-C in Japan. In September 2017, Astellas submitted a Supplemental New Drug Application with the Pharmaceuticals and Medical Devices Agency in Japan for approval to market linaclotide for the additional indication of chronic constipation.

- Ironwood continues to expect the China Food and Drug Administration to complete its review of the filing for approval to market linaclotide in China for adult IBS-C patients in the first quarter of 2018. Ironwood is partnered with AstraZeneca for the development and commercialization of linaclotide in China.

Corporate and Financials

- **Total Revenues**
  - Total revenues were $86.8 million in the third quarter of 2017 compared to $66.1 million in the third quarter of 2016. Included in total revenues was $75.6 million associated with Ironwood's share of the net profits from the sales of LINZESS in the U.S., $9.5 million in sales of linaclotide API to Astellas, linaclotide royalties, co-promotion revenue and ZURAMPIC revenue.
- **Operating Expenses**
  - Operating expenses were $106.3 million in the third quarter of 2017 as compared to $94.4 million in the third quarter of 2016. Operating expenses in the third quarter of 2017 included $6.1 million in cost of revenues, $37.1 million in R&D expenses, $61.8 million in selling, general and administrative (SG&A) expenses, $1.9 million in acquired intangible assets amortization expenses, and a $0.6 million gain on fair value remeasurement of contingent consideration.
  - Contingent consideration and amortization of acquired intangible assets relate to Ironwood's license agreement with AstraZeneca for the exclusive U.S. rights to all products containing lesinurad.
- **Other Expense**
  - **Interest Expense.** Net interest expense was $8.5 million in the third quarter of 2017, primarily in connection with the $150 million 8.375% Notes funded in January 2017 and the approximately $336 million convertible debt financing funded in June 2015. Interest expense recorded in the third quarter of 2017 includes $5.0 million in cash expense and $4.1 million in non-cash expense.
  - **Loss on Derivatives.** Ironwood records a gain/loss on derivatives related to the change in fair value of the convertible note hedges and note hedge warrants issued in connection with the convertible debt financing funded in June 2015. A loss on derivatives of $4.3 million was recorded in the third quarter of 2017.
- **Net Loss**
  - GAAP net loss was $32.3 million, or $0.22 per share, in the third quarter of 2017, compared to $33.2 million, or $0.23 per share, in the third quarter of 2016.
  - Non-GAAP net loss was $26.7 million, or $0.18 per share, in the third quarter of 2017, compared to $25.9 million, or $0.18 per share, in the third quarter of 2016. Non-GAAP net loss excludes the impact of mark-to-market adjustments on the derivatives related to Ironwood's convertible debt, as well as the amortization of acquired intangible assets and the fair value remeasurement of contingent consideration related to Ironwood's U.S. lesinurad license. See Non-GAAP Financial Measures below.
- **Cash Position**
  - Ironwood ended the third quarter of 2017 with $225.4 million of cash, cash equivalents and available-for-sale securities. Ironwood used approximately $31.2 million of cash for operations during the third quarter of 2017.
- **2017 Financial Guidance**
  - Ironwood now expects:
    - R&D expenses to be in the low-to-middle end of the previously guided $145 million to $160 million range;
    - SG&A expenses to be in the low-to-middle end of the previously guided $235 million to $250 million range;
    - the combined Allergan and Ironwood total 2017 marketing and sales expenses for LINZESS to be in the middle of the previously guided $250 million to $280 million range; and

- to use less than $110 million in cash for operations in 2017, up from less than $100 million previously guided.
- Ironwood continues to expect net interest expense to be approximately $40 million.

Non-GAAP Financial Measures

The company presents non-GAAP net loss and non-GAAP net loss per share to exclude the impact of net gains and losses on the derivatives related to our convertible notes that are required to be marked-to-market, as well as the amortization of acquired intangible assets and the fair value remeasurement of contingent consideration associated with Ironwood's U.S. license agreement with AstraZeneca for the exclusive rights to all products containing lesinurad. The derivative gains and losses may be highly variable, difficult to predict and of a size that could have a substantial impact on the company's reported results of operations in any given period. The acquired intangible assets are valued as of the date of acquisition and are amortized over their estimated economic useful life, and management believes excluding the amortization of acquired intangible assets provides more consistency with the treatment of internally developed intangible assets for which research and development costs were previously expensed. The contingent consideration balance is remeasured each reporting period, and the resulting change in fair value impacts the company's reported results of operations. The changes in the fair value remeasurement of contingent consideration do not correlate to the company's actual cash payment obligations in the relevant period. Management believes this non-GAAP information is useful for investors, taken in conjunction with Ironwood's GAAP financial statements, because it provides greater transparency and period-over-period comparability with respect to Ironwood's operating performance. These measures are also used by management to assess the performance of the business. Investors should consider these non-GAAP measures only as a supplement to, not as a substitute for or as superior to, measures of financial performance prepared in accordance with GAAP. In addition, these non-GAAP financial measures are unlikely to be comparable with non-GAAP information provided by other companies. For a reconciliation of these non-GAAP financial measures to the most comparable GAAP measures, please refer to the table at the end of this press release.

Conference Call Information

Ironwood will host a conference call and webcast at 8:30 a.m. Eastern Time on Thursday, November 2, 2017 to discuss its third quarter of 2017 results and recent business activities. 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 1071726. 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 at approximately 11:30 a.m. Eastern Time, on November 2, 2017 running through 11:59 p.m. Eastern Time on November 9, 2017. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 1071726. The archived webcast will be available on Ironwood's website for 14 days beginning approximately one hour after the call has completed.

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 for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid (sUA) levels with a medically appropriate daily dose of a xanthine oxidase inhibitor (XOI) alone. 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.

About LINZESS (linaclotide)

LINZESS® is the #1 prescribed brand for the treatment of adult patients with irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC), based on QuintilesIMS data. Since its FDA approval in August of 2012 and subsequent launch in December 2012, greater than 1.5 million unique patients have filled more than 9 million prescriptions for LINZESS, according to QuintilesIMS.

LINZESS is a once-daily capsule that helps relieve the abdominal pain and constipation associated with IBS-C, as well as the constipation, infrequent stools, hard stools, straining, and incomplete evacuation associated with CIC. The recommended dose is 290 mcg for IBS-C patients and 145 mcg for CIC patients, with a 72 mcg dose approved for use in CIC depending on

individual patient presentation or tolerability. LINZESS should be taken at least 30 minutes before the first meal of the day.

LINZESS is contraindicated in pediatric patients less than 6 years of age. The safety and effectiveness of LINZESS in pediatric patients less than 18 years of age have not been established. In neonatal mice, linaclotide increased fluid secretion as a consequence of GC-C agonism resulting in mortality within the first 24 hours due to dehydration. Due to increased intestinal expression of GC-C, patients less than 6 years of age may be more likely than patients 6 years if age and older to develop severe diarrhea and its potentially serious consequences. In adults with IBS-C or CIC treated with LINZESS, the most commonly reported adverse event was diarrhea.

LINZESS is not a laxative; it is the first medicine approved by the FDA in a class called guanylate cyclase-C (GC-C) agonists. LINZESS contains a peptide called linaclotide that activates the GC-C receptor in the intestine. Activation of GC-C is thought to result in increased intestinal fluid secretion and accelerated transit and a decrease in the activity of pain-sensing nerves in the intestine. The clinical relevance of the effect on pain fibers, which is based on nonclinical studies, has not been established.

In the United States, Ironwood and Allergan plc co-develop and co-commercialize LINZESS for the treatment of adults with IBS-C or CIC. In Europe, Allergan markets linaclotide under the brand name CONSTELLA® for the treatment of adults with moderate to severe IBS-C. In Japan, Ironwood's partner Astellas markets linaclotide under the brand name LINZESS for the treatment of adults with IBS-C. Ironwood also has partnered with AstraZeneca for development and commercialization of linaclotide in China, and with Allergan for development and commercialization of linaclotide in all other territories worldwide.

About ZURAMPIC (lesinurad) 200mg tablets

ZURAMPIC (lesinurad) works in combination with xanthine oxidase inhibitors (XOIs) to treat 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 uric acid transporter 1 (URAT1) and organic anion transporter 4 (OAT4), involved in uric acid reabsorption in the kidney. 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. The boxed warning for ZURAMPIC states that acute renal failure has occurred with ZURAMPIC and was more common when ZURAMPIC was given alone and reinforces that ZURAMPIC should be used in combination with an XOI.

About DUZALLO (lesinurad and allopurinol)

DUZALLO (lesinurad and allopurinol) is a once-daily oral therapy that contains lesinurad 200 mg plus allopurinol 300 mg; it is also available in a lesinurad 200 mg plus allopurinol 200 mg dosage. DUZALLO is approved by the FDA as a once-daily oral treatment for hyperuricemia associated with gout in patients who have not achieved target serum uric acid (sUA) levels with a medically appropriate daily dose of allopurinol alone. DUZALLO is not recommended for the treatment of asymptomatic hyperuricemia. Allopurinol is an XOI whose action differs from that of uricosuric agents such as lesinurad. Allopurinol reduces the production of uric acid (UA); lesinurad increases renal excretion of UA by selectively inhibiting the action of URAT1, the UA transporter responsible for the majority of renal UA reabsorption. The dual-mechanism combination of DUZALLO can address both inefficient excretion and overproduction of UA, thereby lowering sUA levels. DUZALLO should be taken in the morning with food and water, and patients should be advised to stay well hydrated when taking DUZALLO (about 2 liters of liquid a day).

LINZESS Important Safety Information

INDICATIONS AND USAGE

LINZESS (linaclotide) is indicated in adults for the treatment of both irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC).

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS DEHYDRATION IN PEDIATRIC PATIENTS

LINZESS is contraindicated in patients less than 6 years of age. In nonclinical studies in neonatal mice, administration of a single, clinically relevant adult oral dose of linaclotide caused deaths due to dehydration. Use of LINZESS should be avoided in patients 6 years to less than 18 years of age. The safety and effectiveness of LINZESS have not been established in patients less than 18 years of age.

Contraindications

- LINZESS is contraindicated in patients less than 6 years of age due to the risk of serious dehydration.
- LINZESS is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

Warnings and Precautions
Pediatric Risk

- LINZESS is contraindicated in patients less than 6 years of age. The safety and effectiveness of LINZESS in patients less than 18 years of age have not been established. In neonatal mice, linaclotide increased fluid secretion as a consequence of GC-C agonism resulting in mortality within the first 24 hours due to dehydration. Due to increased intestinal expression of GC-C, patients less than 6 years of age may be more likely than patients 6 years of age and older to develop severe diarrhea and its potentially serious consequences.
- Use of LINZESS should be avoided in pediatric patients 6 years to less than 18 years of age. Although there were no deaths in older juvenile mice, given the deaths in young juvenile mice and the lack of clinical safety and efficacy data in pediatric patients, use of LINZESS should be avoided in pediatric patients 6 years to less than 18 years of age.

Diarrhea

- Diarrhea was the most common adverse reaction in LINZESS-treated patients in the pooled IBS-C and CIC double-blind placebo-controlled trials. The incidence of diarrhea was similar in the IBS-C and CIC populations. Severe diarrhea was reported in 2% of 145 mcg and 290 mcg LINZESS-treated patients, and in < 1% of 72 mcg LINZESS-treated CIC patients. If severe diarrhea occurs, dosing should be suspended and the patient rehydrated.

Common Adverse Reactions (incidence ≥2% and greater than placebo)

- In IBS-C clinical trials: diarrhea (20% vs 3% placebo), abdominal pain (7% vs 5%), flatulence (4% vs 2%), headache (4% vs 3%), viral gastroenteritis (3% vs 1%) and abdominal distension (2% vs 1%).
- In CIC trials of a 145 mcg dose: diarrhea (16% vs 5% placebo), abdominal pain (7% vs 6%), flatulence (6% vs 5%), upper respiratory tract infection (5% vs 4%), sinusitis (3% vs 2%) and abdominal distension (3% vs 2%). In a CIC trial of a 72 mcg dose: diarrhea (19% vs 7% placebo) and abdominal distension (2% vs < 1%).

Please see full Prescribing Information including Boxed Warning: http://www.allergan.com/assets/pdf/linzess_pi

ZURAMPIC Important Safety Information and Limitations of Use

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, at: http://www.azpicentral.com/zurampic/zurampic.pdf.

DUZALLO Important Safety Information

WARNING: RISK OF ACUTE RENAL FAILURE

- **Acute renal failure has occurred with lesinurad, one of the components of DUZALLO**

Contraindications:

- Severe renal impairment (estimated creatinine clearance [eCLcr] < 30 mL/min), end-stage renal disease, kidney transplant recipients, or patients on dialysis
- Tumor lysis syndrome or Lesch-Nyhan syndrome
- Known hypersensitivity to allopurinol, including previous occurrence of skin rash

Warnings and Precautions:

- **Renal events:** Adverse reactions related to renal function, including acute renal failure, can occur after initiating DUZALLO. Renal function should be evaluated prior to initiation of DUZALLO and periodically thereafter, as clinically indicated. More frequent renal function monitoring is recommended in patients with eCLcr < 60 mL/min or with serum creatinine elevations 1.5 to 2 times the value when lesinurad treatment was initiated. DUZALLO should not be initiated in patients with an eCLcr < 45 mL/min. Interrupt treatment with DUZALLO if serum creatinine is elevated to > 2 times the pretreatment value or if there are symptoms that may indicate acute uric acid nephropathy, including flank pain, nausea, or vomiting. DUZALLO should not be restarted without another explanation for the serum creatinine abnormalities
- **Skin rash and hypersensitivity:** Skin rash is a frequently reported adverse event in patients taking allopurinol. In some instances, a skin rash may be followed by more severe hypersensitivity reactions associated with exfoliation, fever, lymphadenopathy, arthralgia, and/or eosinophilia including Stevens-Johnson syndrome and toxic epidermal necrolysis. Associated vasculitis and tissue response may be manifested in various ways including hepatitis, renal impairment, seizures, and on rare occasions, death. Hypersensitivity reactions to allopurinol may be increased in patients with decreased renal function who are receiving thiazide diuretics and DUZALLO concurrently. DUZALLO should be discontinued immediately at the first appearance of skin rash or other signs that may indicate an allergic reaction, and additional medical care should be provided as needed
- **Hepatotoxicity:** A few cases of reversible clinical hepatotoxicity have been reported in patients taking allopurinol and, in some patients, asymptomatic rises in serum alkaline phosphatase or serum transaminase have been observed. If anorexia, weight loss, or pruritus develops in patients taking DUZALLO, evaluation of liver function should be performed. In patients with preexisting liver disease, periodic liver function tests are recommended
- **Cardiovascular events:** In clinical trials, major adverse cardiovascular events (defined as cardiovascular deaths,

nonfatal myocardial infarctions, and nonfatal strokes) were observed with DUZALLO. A causal relationship has not been established

- **Bone marrow depression:** Bone marrow depression has been reported in patients receiving allopurinol, most of whom received concomitant drugs with the potential for causing this reaction. This has occurred as early as 6 weeks to as long as 6 years after the initiation of allopurinol therapy. Rarely, a patient may develop varying degrees of bone marrow depression, affecting one or more cell lines, while receiving allopurinol alone. Patients taking allopurinol and mercaptopurine or azathioprine require a reduction in dose to approximately one-third to one-fourth of the usual dose of mercaptopurine or azathioprine
- **Increase in prothrombin time:** It has been reported that allopurinol prolongs the half-life of dicumarol, a coumarin anticoagulant. The prothrombin time should be reassessed periodically in patients receiving coumarin anticoagulants (dicumarol, warfarin) concomitantly with DUZALLO
- **Drowsiness:** Occasional occurrence of drowsiness was reported in patients taking allopurinol. Patients should be alerted to the need for caution when engaging in activities where alertness is mandatory

Adverse Reactions:

- The most common adverse reactions in controlled studies (occurring in 2% or more of patients on lesinurad in combination with allopurinol and at least 1% greater than observed in patients on allopurinol alone) were headache, influenza, blood creatinine increased, and gastroesophageal reflux disease
- The most common adverse reactions identified during post-approval use of allopurinol are skin rash, nausea, and diarrhea

Indication and Limitations of Use:

DUZALLO, a combination of lesinurad, a URAT1 inhibitor, and allopurinol, a xanthine oxidase inhibitor, is indicated for the treatment of hyperuricemia associated with gout in patients who have not achieved target serum uric acid levels with a medically appropriate daily dose of allopurinol alone.

- DUZALLO is not recommended for the treatment of asymptomatic hyperuricemia

Please see full Prescribing Information, including Boxed, at
https://www.irwdpi.com/duzallo/DuzalloPIandMedguide2017.pdf#page=1

This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including statements about the development, launch, commercial availability and commercial potential of linaclotide, lesinurad, our product candidates and the other products that we promote and the drivers, timing, impact and results thereof; market size, prevalence, growth and opportunity, including peak sales (and drivers thereof) and the growth in and potential demand for linaclotide, lesinurad and our product candidates, as well as their potential impact on applicable markets; the potential indications for, and benefits of, linaclotide, lesinurad and our product candidates; the anticipated timing of preclinical, clinical and regulatory developments (including strengthening the clinical profile and expanding the clinical utility of linaclotide) and the design, timing and results of clinical and preclinical studies; the potential for, and timing of, regulatory submissions and approvals for linaclotide, lesinurad and our product candidates; expected periods of patent exclusivity and life of the respective patent portfolios for linaclotide, lesinurad and our product candidates; commercial strategy; the strength of the intellectual property protection for linaclotide, lesinurad and our product candidates and our intentions and efforts to protect such intellectual property; and our financial performance and results, and guidance and expectations related thereto (including the drivers and timing thereof), including expectations related to Ironwood revenue CAGR and revenue growth, positive cash flow, LINZESS U.S. net sales, commercial margin, ex-U.S. revenue, allocation of capital, R&D, SG&A and marketing and sales expenses, net interest expense and cash used for operations. 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 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; efficacy, safety and tolerability of linaclotide, lesinurad and our product candidates; decisions by regulatory authorities; the risk that we are unable to successfully integrate lesinurad into our existing business, commercialize lesinurad or realize the anticipated benefits of the lesinurad transaction; the risk that we may never get sufficient patent protection for linaclotide, lesinurad and our product candidates or that we are not able to successfully protect such patents; the outcomes in legal proceedings to protect or enforce the patents relating to our products and product candidates,

including ANDA litigation; 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 company revenues, linaclotide, lesinurad or our product candidates; the risk that we are unable to manage our operating expenses or cash use for operations, or are unable to commercialize our products, within the guided ranges or otherwise as expected; and the risks listed under the heading "Risk Factors" and elsewhere in Ironwood's Quarterly Report on Form 10-Q for the quarter ended June 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. Further, Ironwood considers the net profit for the U.S. LINZESS brand collaboration with Allergan in assessing the product's performance and calculates it based on inputs from both Ironwood and Allergan. This figure should not be considered a substitute for Ironwood's GAAP financial results. An explanation of our calculation of this figure is provided in the U.S. LINZESS Brand Collaboration table and related footnotes accompanying this press release.

Condensed Consolidated Balance Sheets
(In thousands)
(unaudited)

	September 30, 2017	December 31, 2016
Assets		
Cash, cash equivalents and available-for-sale securities	$ 225,417	$ 305,216
Accounts receivable, net	80,083	64,854
Inventory	479	1,081
Prepaid expenses and other current assets	8,074	9,030
Total current assets	314,053	380,181
Property and equipment, net	17,175	20,512
Convertible note hedges	121,836	132,521
Intangible assets, net	163,381	166,119
Goodwill	785	785
Other assets	7,856	9,703
Total assets	$ 625,086	$ 709,821
Liabilities and Stockholders' (Deficit) Equity		
Accounts payable, accrued expenses and other current liabilities	$ 59,184	$ 62,941
Current portion of capital lease obligations	4,411	6,227
Current portion of deferred rent	195	7,719
Current portion of contingent consideration	699	14,244
Total current liabilities	64,489	91,131
Capital lease obligations	-	82
Deferred rent, net of current portion	4,484	557
Other liabilities	8,190	8,190
Contingent consideration, net of current portion	69,830	63,416
Note hedge warrants	103,743	113,237
Convertible notes	245,324	234,243
Long-term debt	146,605	132,249
Total stockholders' (deficit) equity	(17,579)	66,716
Total liabilities and stockholders' (deficit) equity	$ 625,086	$ 709,821

Condensed Consolidated Statements of Operations
(In thousands, except per share amounts)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Total revenues	$ 86,825	$ 66,106	$ 204,068	$186,498
Cost and expenses:				

Cost of revenues, excluding amortization of acquired intangible assets	6,080	-	10,113	-
Write-down of lesinurad commercial supply to net realizable value	71	-	167	-
Research and development	37,065	37,526	108,111	101,050
Selling, general and administrative	61,774	44,987	175,170	118,073
Amortization of acquired intangible assets	1,897	3,213	2,738	4,278
(Gain) loss on fair value remeasurement of contingent consideration	(628)	8,667	7,919	8,667
Total cost and expenses	106,259	94,393	304,218	232,068
Loss from operations	(19,434)	(28,287)	(100,150)	(45,570)
Other (expense) income:				
Interest expense, net	(8,534)	(9,458)	(25,672)	(28,676)
Loss on extinguishment of debt	-	-	(2,009)	-
(Loss) gain on derivatives	(4,329)	4,541	(1,191)	6,043
Other expense, net	(12,863)	(4,917)	(28,872)	(22,633)
GAAP net loss	$ (32,297)	$ (33,204)	$(129,022)	$ (68,203)
GAAP net loss per share—basic and diluted	$ (0.22)	$ (0.23)	$ (0.87)	$ (0.47)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Non-GAAP net loss	$ (26,699)	$ (25,865)	$(117,174)	$ (61,301)
Non-GAAP net loss per share (basic and diluted)	$ (0.18)	$ (0.18)	$ (0.79)	$ (0.42)
Weighted average number of common shares used in net loss per share — basic	149,502	145,180	148,695	144,474

Reconciliation of GAAP Results to Non-GAAP Financial Measures
(In thousands, except per share amounts)
(unaudited)

A reconciliation between net loss on a GAAP basis and on a non-GAAP basis is as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
GAAP net loss	$ (32,297)	$ (33,204)	$(129,022)	$(68,203)
Adjustments:				
Mark-to-market adjustments on the derivatives related to convertible notes, net	4,329	(4,541)	1,191	(6,043)
Amortization of intangible assets	1,897	3,213	2,738	4,278
Fair value remeasurement of contingent consideration	(628)	8,667	7,919	8,667
Non-GAAP net loss	$ (26,699)	$ (25,865)	$(117,174)	$(61,301)

A reconciliation between diluted net loss per share on a GAAP basis and on a non-GAAP basis is as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
GAAP net loss per share - Basic and Diluted	$ (0.22)	$ (0.23)	$ (0.87)	$ (0.47)
Adjustments to GAAP net loss per share (as detailed above)	0.04	0.05	0.08	0.05
Non-GAAP net loss per share - basic and diluted	$ (0.18)	$ (0.18)	$ (0.79)	$ (0.42)

U.S. LINZESS Brand Collaboration[1]
Revenue/Expense Calculation
(In thousands)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	**2016**	**2017**	**2016**
LINZESS U.S. net sales	$ 190,932	$ 164,379	$ 506,380	$ 451,980
Commercial costs and expenses[2]	64,034	64,136	215,174	197,841
Commercial profit on sales of LINZESS	$ 126,898	$ 100,243	$ 291,206	$ 254,139
Commercial Margin[3]	*66%*	*61%*	*58%*	*56%*
Ironwood's share of net profit	$ 63,449	$ 50,122	$ 145,603	$ 127,070
Ironwood's selling, general and administrative expenses[4]	10,456	7,491	34,061	25,523
Profit share adjustment[5]	1,677	2,370	1,677	2,370
Ironwood's collaborative arrangement revenue	$ 75,582	$ 59,983	$ 181,341	$ 154,963

[1] Ironwood collaborates with Allergan on the development and commercialization of linaclotide in North America. Under the terms of the collaboration agreement, Ironwood receives 50% of the net profits and bears 50% of the net losses from the commercial sale of LINZESS in the U.S. The purpose of this table is to present calculations of Ironwood's share of net profit (loss) generated from the sales of LINZESS in the U.S. and Ironwood's collaboration revenue/expense; however, the table does not present the research and development expenses related to LINZESS in the U.S. that are shared equally between the parties under the collaboration agreement. For the three months ended September 30, 2017, net profit for the U.S. LINZESS brand collaboration with Allergan was $111.0 million, calculated by subtracting $64.0 million in commercial costs and expenses and $15.9 million in research and development expenses, from LINZESS U.S. net sales of $190.9 million.

[2] Includes cost of goods sold incurred by Allergan as well as selling, general and administrative expenses incurred by Allergan and Ironwood that are attributable to the cost-sharing arrangement between the parties.

[3] Commercial margin is defined as commercial profit on sales of LINZESS as a percent of total LINZESS U.S. net sales.

[4] Includes Ironwood's selling, general and administrative expenses attributable to the cost-sharing arrangement with Allergan.

[5] Ironwood or Allergan may recognize additional revenue or incur additional expenses resulting in an adjustment to the company's share of the net profits as stipulated by the collaboration agreement.

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