Ironwood Pharmaceuticals Provides First Quarter 2018 Investor Update

May 1, 2018

– First quarter revenue increased 33% year-over-year to $69 million, driven primarily by LINZESS® (linaclotide) U.S. net sales of $159 million and commercial margin of 63% –

– IW-3718 Phase III program expected to initiate in the third quarter of 2018 –

– Phase II sGC programs, praliciguat and olinciguat (IW-1701) continue to progress –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 1, 2018-- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD), a commercial biotechnology company, today provided an update on its first quarter 2018 results and recent business activities.

"Ironwood's first quarter results reflect year-over-year topline growth of 33%, significant commercial and pipeline progress, and continued financial discipline," said Peter Hecht, chief executive officer of Ironwood. "LINZESS continued to demonstrate strong demand, with 15% year-over-year prescription volume growth. We believe we have alignment on Phase III design for IW-3718 following a productive end of Phase II meeting with the FDA and expect to initiate the IW-3718 trials in the third quarter of 2018. In addition, we continue to make good progress advancing our four Phase II trials with praliciguat and olinciguat, our lead clinical sGC stimulators."

First Quarter 2018 and Recent Highlights

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

- *U.S. LINZESS.* U.S. net sales, as reported by Ironwood's U.S. collaboration partner Allergan plc, were $159.3 million in the first quarter of 2018, an 8% increase compared to the first quarter of 2017. Ironwood and Allergan share equally in brand collaboration profits.
    - LINZESS commercial margin was 63% in the first quarter of 2018 compared to 52% in the first quarter of 2017.
    - Net profit for the LINZESS U.S. brand collaboration, net of commercial and research and development (R&D) expenses, was $88.8 million in the first quarter of 2018, a 43% increase compared to the first quarter of 2017.
    - Total LINZESS prescription volume in the first quarter of 2018 included approximately 30 million LINZESS capsules, an 15% increase in capsules compared to the first quarter of 2017, per IQVIA.
    - More than 764,000 total LINZESS prescriptions were filled in the first quarter of 2018, an approximately 9% increase compared to the first quarter of 2017, per IQVIA.
    - Since the launch of LINZESS in December 2012, greater than 2 million unique patients have filled approximately 10.6 million prescriptions, per IQVIA.
- In January 2018, Ironwood and Allergan reached an agreement with wholly-owned subsidiaries of Sun Pharmaceutical Industries Ltd. (Sun Pharma, including its subsidiaries and/or associated companies), resolving patent litigation brought in response to Sun Pharma's abbreviated new drug application (ANDA) seeking approval to market a generic version of LINZESS prior to the expiration of the companies' patents. Pursuant to the terms of the settlement, Ironwood and Allergan will grant the wholly-owned subsidiaries of Sun Pharma a license to market a generic version of LINZESS in the U.S. beginning on February 1, 2031 (subject to U.S. FDA approval), unless certain limited circumstances, customary for settlement agreements of this nature, occur. As a result of the settlement, all Hatch-Waxman litigation between the companies and Sun Pharma regarding LINZESS patents has been dismissed.
- *Additional Abdominal Symptom Claims.* Ironwood and Allergan expect to initiate a single Phase III trial with LINZESS in mid-2018 to evaluate its efficacy for relief of additional abdominal symptoms, including bloating and discomfort, two highly bothersome symptoms associated with IBS-C.
- *Linaclotide Delayed Release.* An estimated 20 to 25 million patients suffer from IBS-mixed and IBS with diarrhea in the U.S. Ironwood and Allergan plan to advance into a Phase IIb clinical trial a linaclotide delayed release formulation as a potential visceral, non-opioid, pain-relieving agent for patients suffering from all subtypes of IBS. The companies are in active discussions with the U.S. FDA about this program.
- *LINZESS-Japan.* Ironwood reported $5.4 million in sales of linaclotide active pharmaceutical ingredient (API) to its Japanese partner, Astellas Pharma Inc. in the first quarter of 2018.

Uncontrolled Gout

- *DUZALLO® (lesinurad and allopurinol)* and *ZURAMPIC® (lesinurad).* Ironwood is systematically exploring a more

comprehensive marketing mix for its lesinurad franchise, including DUZALLO and ZURAMPIC, in select test markets (with paired controls), while continuing to expand affordable access across the country. The data received from these test markets in 2018 are expected to inform our lesinurad franchise investment decisions. Combined U.S. net sales were $0.6 million in the first quarter of 2018.

Persistent Gastroesophageal Reflux Disease (GERD)

- *IW-3718*. Ironwood is actively working to advance IW-3718, its gastric retentive formulation of a bile acid sequestrant for the potential treatment of persistent GERD, into Phase III trials. There are an estimated 10 million Americans who suffer regularly from symptoms of persistent GERD, such as heartburn and regurgitation, despite receiving treatment with the current standard of care, proton pump inhibitors.
    - Following a series of productive meetings with the U.S. FDA, Ironwood expects to initiate two randomized, placebo-controlled Phase III trials for IW-3718 in the third quarter of 2018. These trials are expected to evaluate the safety and efficacy of IW-3718 1500mg in patients with persistent GERD. The two trials are expected to enroll less than 800 patients each, with heartburn severity response as the primary endpoint. Further details on study design and endpoints will be provided upon the initiation of the trials.

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

- *Praliciguat (IW-1973).* Ironwood is enrolling patients in Phase II tirals to evaluate praliciguat, its lead soluble guanylate cyclase (sGC) stimulator, for the potential treatment of serious diseases, including 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 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, with no approved treatments available.
    - *Diabetic nephropathy.* Ironwood expects to enroll approximately 150 patients into a randomized, double-blind, placebo-controlled, dose-ranging Phase II trial designed to evaluate the safety and efficacy of praliciguat in patients with diabetic nephropathy.
    - *HFpEF.* Ironwood expects to enroll approximately 325 patients into a randomized, double-blind, placebo-controlled, dose-ranging Phase II trial designed to evaluate the safety and efficacy of praliciguat in patients with HFpEF.

Sickle Cell Disease and Achalasia

- *Olinciguat (IW-1701).* Ironwood is enrolling patients in Phase II trials to evaluate olinciguat, its second clinical sGC stimulator, for the potential treatment of sickle cell disease and of achalasia. Sickle cell disease is a rare, debilitating genetic disorder that affects approximately 100,000 Americans and causes red blood cells to become sickle-shaped, reducing normal red blood cell number. Achalasia is a rare disease with a prevalence rate of 10/100,000 Americans in which the lower esophagus does not relax normally, causing dysphagia (swallowing problems), regurgitation, and chest pain.
    - *Sickle Cell Disease*. Ironwood expects to enroll approximately 80 patients into a multicenter, randomized, double-blind, placebo-controlled, dose-ranging Phase II trial of olinciguat in patients with sickle cell disease. The Phase II trial is designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of olinciguat in these patients.
    - *Achalasia.* Ironwood continues to enroll patients into a randomized, double-blind, placebo-controlled, single-dose Phase IIa study of olinciguat in patients with achalasia. This study is designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of olinciguat in these patients. Data from this study are expected in 2018.

Corporate and Financials

- **Total Revenues**
    - Total revenues were $69.2 million in the first quarter of 2018 compared to $52.2 million in the first quarter of 2017. Included in total revenues was $61.2 million associated with Ironwood's share of the net profits from the sales of LINZESS in the U.S., $5.4 million in sales of linaclotide API to Astellas, $0.6 million in ZURAMPIC and DUZALLO product revenue, and $2.0 million in linaclotide royalties, co-promotion and other revenue.
- **Operating Expenses**
    - Operating expenses were $105.0 million in the first quarter of 2018, compared to $91.8 million in the first quarter of 2017. Operating expenses in the first quarter of 2018 included $2.6 million in cost of revenues, $36.5 million in R&D expenses, $61.9 million in selling, general and administrative (SG&A) expenses, of which $2.4 million related to Ironwood's field-based workforce reduction in January 2018, $3.5 million in acquired intangible assets amortization expenses, and a $0.5 million loss 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 $8.6 million in the first quarter of 2018, 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 first quarter of 2018 includes $5.0 million in cash expense and $4.2 million in non-cash expense.
  - **Gain on Derivatives.** Ironwood recorded a gain 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 gain on derivatives of $1.3 million was recorded in the first quarter of 2018.
- **Net Loss**
  - GAAP net loss was $43.1 million, or $0.29 per share, in the first quarter of 2018, compared to a net loss of $52.5 million, or $0.36 per share, in the first quarter of 2017.
  - Non-GAAP net loss was $40.5 million, or $0.27 per share, in the first quarter of 2018, compared to $48.3 million, or $0.33 per share, in the first quarter of 2017. 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 first quarter of 2018 with approximately $194.4 million of cash, cash equivalents and available-for-sale securities. Ironwood used approximately $30.9 million of cash for operations during the first quarter of 2018.

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 Tuesday, May 1, 2018 to discuss its first quarter 2018 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 9859406. 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 May 1, 2018 running through 11:59 p.m. Eastern Time on May 8, 2018. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 9859406. 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 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.

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 IQVIA data. Since its FDA approval in August of 2012 and subsequent launch in December 2012, greater than 2 million unique patients have filled approximately 10.6 million prescriptions for LINZESS, according to IQVIA.

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 of 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://irwdpi.com/zurampic/ZURAMPIC_PI_and_Medguide_2017.pdf#page=1

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, other product candidates and the other products that we promote and the drivers, timing, impact and results thereof; market size, prevalence, growth and opportunity, and the growth in, and potential demand for, linaclotide, lesinurad and other product candidates, as well as their potential impact on applicable markets; the potential indications for, and benefits of, linaclotide, lesinurad and other product candidates; the anticipated timing of preclinical, clinical and regulatory developments and the design, timing and results of clinical and preclinical studies; expected periods of patent exclusivity, durability and life of the respective patent portfolios for linaclotide, lesinurad and other product candidates; and the strength of the intellectual property protection for linaclotide, lesinurad and other product candidates and our intentions and efforts to protect such intellectual property.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 other product candidates; decisions by regulatory and judicial authorities; the risk that we are unable to successfully 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 other 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 other 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 Annual Report on Form 10-K for the year ended December 31, 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)

	March 31, 2018	December 31, 2017
Assets		
Cash, cash equivalents and available-for-sale securities	$ 194,447	$ 221,416
Accounts receivable, net	70,651	82,157
Inventory	1,705	735
Prepaid expenses and other current assets	8,924	7,288
Total current assets	275,727	311,596
Restricted cash	7,056	7,056
Property and equipment, net	16,844	17,274
Convertible note hedges	113,445	108,188
Intangible assets, net	156,429	159,905
Goodwill	785	785
Other assets	809	870
Total assets	$ 571,095	$ 605,674
Liabilities and Stockholders' (Deficit) Equity		
Accounts payable, accrued expenses and other current liabilities	$ 46,427	$ 61,508
Current portion of capital lease obligations	3,359	4,077
Current portion of deferred rent	237	195
Current portion of long- term debt	11,958	-
Current portion of contingent consideration	355	247
Total current liabilities	62,336	66,027
Deferred rent, net of current portion	5,860	5,449
Other liabilities	5,060	5,060

Contingent consideration, net of current portion	31,389	31,011
Note hedge warrants	96,129	92,188
Convertible notes	253,153	249,193
Long-term debt	135,220	146,898
Total stockholders' (deficit) equity	(18,052)	9,848
Total liabilities and stockholders' (deficit) equity	$ 571,095	$ 605,674

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

	Three Months Ended March 31,	
	2018	**2017**
Total revenues	69,155	$ 52,166
Cost and expenses:		
Cost of revenues, excluding amortization of acquired intangible assets	2,607	531
Research and development	36,505	33,702
Selling, general and administrative	61,923	55,604
Amortization of acquired intangible assets	3,476	420
Loss on fair value remeasurement of contingent consideration	512	1,614
Total cost and expenses	105,023	91,871
Loss from operations	(35,868)	(39,705)
Other (expense) income:		
Interest expense, net	(8,592)	(8,588)
Gain (loss) on derivatives	1,316	(2,199)
Loss on extinguishment of debt	-	(2,009)
Other expense, net	(7,276)	(12,796)
GAAP net loss	$ (43,144)	$ (52,501)
GAAP net loss per share—basic and diluted	$ (0.29)	$ (0.36)

	Three Months Ended March 31,	
	2018	**2017**
Non-GAAP net loss	$ (40,472)	$ (48,268)
Non-GAAP net loss per share (basic and diluted)	$ (0.27)	$ (0.33)
Weighted average number of common shares used in net loss per share — basic and diluted	151,013	147,786

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 March 31,	
	2018	**2017**
GAAP net loss	$ (43,144)	$ (52,501)
Adjustments:		

Mark-to-market adjustments on the derivatives related to convertible notes, net	(1,316)	2,199
Amortization of intangible assets	3,476	420
Loss on fair value remeasurement of contingent consideration	512	1,614
Non-GAAP net loss	(40,472)	$ (48,268)

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

	Three Months Ended March 31,	
	2018	**2017**
GAAP net loss per share – Basic and Diluted	$ (0.29)	$ (0.36)
Adjustments to GAAP net loss per share (as detailed above)	0.02	0.03
Non-GAAP net loss per share – basic and diluted	$ (0.27)	$ (0.33)

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

	Three Months Ended March 31,	
	2018	**2017**
LINZESS U.S. net sales	$ 159,334	$ 147,615
Commercial costs and expenses[2]	58,890	70,929
Commercial profit on sales of LINZESS	$ 100,444	$ 76,686
Commercial Margin[3]	*63%*	*52%*
Ironwood's share of net profit	$ 50,222	$ 38,343
Ironwood's selling, general and administrative expenses [4]	10,928	11,109
Ironwood's collaborative arrangement revenue	$ 61,150	$ 49,452

[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 March 31, 2018, net profit for the U.S. LINZESS brand collaboration with Allergan was $88.8 million, calculated by subtracting $58.9 million in commercial costs and expenses and $11.6 million in research and development expenses, from LINZESS U.S. net sales of $159.3 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.

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