



## Ironwood Pharmaceuticals Provides Third Quarter 2018 Investor Update

November 6, 2018

– LINZESS® (linaclotide) U.S. net sales increased 7% to \$205 million in 3Q 2018 vs 3Q 2017 –

– Ironwood revenue of \$66 million in 3Q 2018, which includes a \$30 million reduction due to LINZESS change in estimate as reported to Ironwood by Allergan –

– Received Fast Track Designation for pralicyquat for potential treatment of HFpEF –

– On track to complete separation of Ironwood into two independent, publicly traded companies in first half 2019 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 6, 2018-- [Ironwood Pharmaceuticals, Inc.](http://IronwoodPharmaceuticals.Inc) (Nasdaq: IRWD), a commercial biotechnology company, today provided an update on its third quarter 2018 results and recent business activities.

"Ironwood carried operating momentum from the first half of 2018 through the third quarter, driven by 12% LINZESS demand growth and further advancement of our five ongoing clinical programs with linaclotide, IW-3718, olinciguat and pralicyquat," said Peter Hecht, chief executive officer of Ironwood. "LINZESS is the branded prescription market leader in its class, driven by our productive investments in marketing, personal promotion and payer access. LINZESS is a growth brand with years of expected patent coverage ahead, and we and Allergan are investing in multiple innovative strategies that we believe represent an opportunity to drive significant growth going forward."

Dr. Hecht continued, "We also made progress on our planned separation, which we believe will better position both companies to bring new treatment options to patients and unlock value for shareholders. Following the separation, we expect Ironwood will be a profitable, leading U.S. GI company. We expect the R&D Co. to harness its expertise in sGC pharmacology, developing five sGC stimulators tailored for serious and orphan diseases."

### Third Quarter 2018 and Recent Highlights

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

- U.S. LINZESS® (linaclotide). U.S. net sales, as reported by Ironwood's U.S. collaboration partner Allergan plc, were \$204.8 million in the third quarter of 2018, a 7% increase compared to the third quarter of 2017. Ironwood and Allergan share equally in U.S. brand collaboration profits.
  - During the third quarter, Allergan reported to Ironwood a \$59.3 million negative adjustment to LINZESS net sales relating to the cumulative difference between Allergan's previous gross-to-net estimates during the three years ended December 31, 2015, 2016 and 2017 and actual subsequent payments made. This equates to between 3-4% of LINZESS net sales for each of those annual periods and is primarily associated with estimated governmental and contractual rebates, as reported to Ironwood by Allergan.
    - Upon receiving the information from Allergan, Ironwood recorded a \$29.7 million reduction to collaborative arrangement revenue and accounts receivable in its third quarter financial statements related to its share of the adjustment. Ironwood's collaborative arrangement revenue related to sales of LINZESS in the U.S. for the third quarter of 2018 was \$52.3 million, down approximately 29% compared to the third quarter of 2017, driven primarily by this reduction.
    - Going forward, Ironwood expects LINZESS brand-specific adjustments to be made by Allergan on a more frequent basis to reduce the potential for multi-year adjustments of this magnitude.
  - LINZESS commercial margin, excluding the \$59.3 million adjustment, was 69% in the third quarter of 2018 compared to 66% in the third quarter of 2017. See U.S. Brand Collaboration table below.
  - Net profit for the LINZESS U.S. brand collaboration, net of commercial and research and development (R&D) expenses and excluding the \$59.3 million adjustment, was \$125.5 million in the third quarter of 2018, a 13% increase compared to the third quarter of 2017. See U.S. Brand Collaboration table below.
  - Total LINZESS prescription volume in the third quarter of 2018 included approximately 33 million LINZESS capsules, an approximately 12% increase in capsules compared to the third quarter of 2017, per IQVIA.
  - More than 830,000 total LINZESS prescriptions were filled in the third quarter of 2018, an approximately 6% increase compared to the third quarter of 2017, per IQVIA.
  - Since the launch of LINZESS in December 2012, approximately 2.5 million unique patients have filled approximately 12 million prescriptions, per IQVIA.
- *Linaclotide Additional Abdominal Symptom Claims*. In July 2018, Ironwood and Allergan initiated a randomized, double-blind, placebo-controlled Phase IIIb trial expected to enroll approximately 600 adult IBS-C patients in the U.S. The trial is

designed to evaluate the efficacy and safety of linaclotide 290 mcg on multiple abdominal symptoms including pain, bloating and discomfort. Eligible patients are being randomized to placebo or linaclotide 290 mcg once daily for 12 weeks, followed by a four-week randomized withdrawal period. The Phase IIIb trial is enrolling faster than expected, and topline data are now expected in mid-2019.

- *MD-7246 (formerly linaclotide delayed release)*. MD-7246 has the potential to be an oral, intestinal, non-opioid, pain-relieving agent for patients in the U.S. suffering from all subtypes of IBS, including IBS-C, IBS with diarrhea and IBS-mixed. A randomized, double-blind, placebo-controlled Phase II trial of MD-7246 is expected to initiate in the first quarter of 2019. This trial is designed to evaluate the safety, tolerability, and treatment effect on abdominal pain of MD-7246 in approximately 400 IBS patients.
- *LINZESS-Japan*. In August 2018, Ironwood and its Japanese partner Astellas Pharma Inc. announced that LINZESS was approved in Japan for the additional indication of chronic constipation, and launched with this indication shortly thereafter. LINZESS was approved for the treatment of IBS-C in Japan in December 2016 and has been on the Japanese market since March 2017. Ironwood reported \$9.5 million in sales of linaclotide active pharmaceutical ingredient (API) to Astellas in the third quarter of 2018.
- *Linaclotide-China*. Ironwood now expects the China Food and Drug Administration (CFDA) to complete its review of the marketing application for linaclotide in China for adult IBS-C patients in early 2019 due to the timing of the CFDA review process. Ironwood is partnered with AstraZeneca AB for the development and commercialization of linaclotide in China.

#### **Persistent Gastroesophageal Reflux Disease (GERD)**

- *IW-3718*. Ironwood is currently enrolling patients in two pivotal Phase III trials to evaluate IW-3718, its gastric retentive formulation of a bile acid sequestrant for the potential treatment of persistent GERD. Persistent GERD affects an estimated 10 million Americans who continue to suffer from heartburn and regurgitation despite receiving treatment with proton pump inhibitors (PPIs), the current standard of care.
  - The Phase III trials are identical randomized, double-blind, placebo-controlled, multicenter trials that target enrolling approximately 1,320 total patients (660 in each trial) with persistent GERD who demonstrate evidence of pathological acid reflux.
  - The primary endpoint of each trial is an overall heartburn response, defined as a patient who experiences at least a 45% reduction from baseline in heartburn severity (an improvement determined to be clinically meaningful based on patient-reported outcomes in the Phase IIb trial) for at least four out of eight weeks, including at least one of the last two weeks.

#### **Sickle Cell Disease**

*Olinciguat*. Ironwood is advancing olinciguat, one of its tailored clinical soluble guanylate cyclase (sGC) stimulators, for the potential treatment of sickle cell disease. Sickle cell disease is a rare, genetic disease that affects approximately 100,000 Americans. It causes red blood cells to "sickle", or become misshapen, and to more easily rupture, resulting in nitric oxide depletion and severe complications including chronic vascular inflammation, painful vaso-occlusive crises, poor blood flow to organs, pulmonary hypertension, and renal failure.

- *Sickle Cell Disease*. Ironwood is enrolling patients in a Phase II multicenter, randomized, double-blind, placebo-controlled, dose-ranging trial designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of once-daily, oral olinciguat in approximately 88 patients with sickle cell disease. Topline data are expected in the second half of 2019.
- *Achalasia*. Ironwood today announces positive data from a small, exploratory Phase IIa single-dose study in patients with type I or type II achalasia in which olinciguat demonstrated the expected pharmacokinetic and pharmacodynamic effects. Data from the Phase IIa study showed that single doses of olinciguat reduced Integrated Relaxation Pressure (IRP), a measure of dilation of the lower esophageal sphincter (LES) during swallowing, relative to baseline. The reduction in IRP observed in this study provides support for sGC target engagement. Data also demonstrated a pharmacokinetic profile of olinciguat supporting once-daily dosing, consistent with findings from previous Phase I data in healthy volunteers. In the study, olinciguat was well tolerated and no serious adverse events (SAEs) were reported. The most common adverse event reported in this trial was mild dizziness. Ironwood intends to focus its resources on olinciguat in sickle cell disease, where there is a significant unmet need and the potential to play a critical role in treating patients. Ironwood will not pursue additional clinical studies in achalasia at this time.

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

- *Praliguat*. Ironwood is advancing praliguat for the potential treatment of diabetic nephropathy and of 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. Ironwood intends to out-license praliguat for development and commercialization to a global partner before entering Phase III trials.
  - *Diabetic nephropathy*. Ironwood is enrolling patients into a randomized, double-blind, placebo-controlled,

dose-ranging Phase II trial designed to evaluate the safety and efficacy of praliguat in patients with diabetic nephropathy. Topline data are expected in the second half of 2019.

- *HFpEF*. In September 2018, the U.S. FDA granted Fast Track Designation for praliguat for the treatment of patients with HFpEF. Ironwood is enrolling patients into a randomized, double-blind, placebo-controlled Phase II trial designed to evaluate the safety and efficacy of the high dose arm of praliguat in patients with HFpEF. Topline data are expected in the second half of 2019.

## Corporate Updates

### • Intent to Separate

- In May 2018, Ironwood announced its intent to separate into two independent, publicly traded companies (Ironwood and "R&D Co."). The separation is expected to be completed in the first half of 2019 and is anticipated to be tax-free to Ironwood shareholders.
  - Following the separation, Ironwood expects to be profitable and to focus on building a leading U.S. GI healthcare company. Ironwood intends to leverage its broad capabilities to advance a strong GI portfolio, including LINZESS – the branded prescription market-leading product in its class – and two potentially highly differentiated, late-stage development products in IW-3718 and MD-7246.
  - R&D Co. expects to harness its deep expertise in cyclic guanosine monophosphate (cGMP) pharmacology to advance an innovative sGC stimulator pipeline focused on the treatment of serious and orphan diseases. At its strategic core are expected to be five novel sGC stimulator programs tailored to the tissues most relevant to the diseases they are designed to treat, including olinciguat, praliguat, IW-6463, and late-stage discovery programs targeting serious liver and lung diseases.

### • Lesinurad U.S. Termination

- In August 2018, Ironwood delivered to AstraZeneca notice of termination of the U.S. lesinurad license agreement, expected to be effective 180 days from the notice.
  - Ironwood expects to save \$75 million to \$100 million in full year 2019 operating expenses, primarily from SG&A.
  - Following the termination notification, Ironwood initiated a reduction in its workforce, primarily consisting of field-based employees. Total costs related to the reduction in workforce, including severance costs, termination fees, and other contract-related costs were approximately \$7.6 million during the third quarter.

## Financial Results

### • Total Revenues

- Total revenues were \$65.7 million in the third quarter of 2018 compared to \$86.8 million in the third quarter of 2017.
  - As noted above, revenues were lower year-over-year primarily due to the \$29.7 million change in estimate recorded to collaborative arrangement revenue as a result of the 2015-2017 LINZESS net sales adjustment, as reported to Ironwood by Allergan.
  - Total revenues consisted of \$52.3 million associated with Ironwood's share of the net profits from the sales of LINZESS in the U.S., including the \$29.7 million reduction, \$10.3 million in sales of linaclotide API, \$1.9 million in linaclotide royalties, co-promotion and other revenue, and \$1.2 million in ZURAMPIC® (lesinurad) and DUZALLO® (lesinurad + allopurinol) product revenue.

### • Operating Expenses

- Operating expenses were \$234.8 million in the third quarter of 2018, compared to \$106.3 million in the third quarter of 2017.
  - Operating expenses were higher year-over-year primarily due to a \$151.8 million non-cash impairment of intangible assets, partially offset by a \$33.5 million non-cash gain on fair value remeasurement of contingent consideration, both related to Ironwood's U.S. lesinurad license agreement with AstraZeneca.
  - Operating expenses in the third quarter of 2018 also consisted of \$55.2 million in SG&A expenses, \$46.8 million in R&D expenses, \$10.3 million in restructuring expenses, \$4.6 million in cost of revenues, and \$1.2 million in acquired intangible assets amortization expenses, partially offset by \$1.6 million related to the write-down of inventory to net realizable value and (settlement) loss on non-cancellable purchase commitments.

### • Other Expense

- **Interest Expense.** Net interest expense was \$8.7 million in the third 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 third quarter of 2018 includes \$5.0 million in cash expense and \$4.5 million in non-cash expense.
- **Gain on Derivatives.** Ironwood recorded a gain on derivatives of \$3.5 million 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.

- **Net Loss**

- GAAP net loss was \$174.4 million, or \$1.14 per share, in the third quarter of 2018, compared to a net loss of \$32.3 million, or \$0.22 per share, in the third quarter of 2017.
- Non-GAAP net loss was \$58.4 million, or \$0.38 per share, in the third quarter of 2018, compared to \$26.7 million, or \$0.18 per share, in the third quarter of 2017. Non-GAAP net loss excludes the impact of mark-to-market adjustments on the derivatives related to Ironwood's convertible debt, the amortization of acquired intangible assets, the fair value remeasurement of contingent consideration related to Ironwood's U.S. lesinurad license, and the impairment of acquired intangible assets in connection with Ironwood's notice of termination of the lesinurad franchise. See Non-GAAP Financial Measures below.

- **Cash Position**

- Ironwood ended the third quarter of 2018 with approximately \$161.4 million of cash, cash equivalents and available-for-sale securities. Ironwood used approximately \$26.6 million of cash for operations during the third quarter of 2018.

- **2018 Financial Guidance**

Ironwood continues to expect in 2018:

- SG&A expenses to be in the range of \$230 million to \$250 million;
- R&D expenses to be in the range of \$160 million to \$180 million;
- the combined Ironwood and Allergan total marketing and sales expenses for LINZESS to be in the range of \$230 to \$260 million; and,
- net interest expense to be less than \$40 million.

Ironwood now expects total restructuring costs to be approximately \$16 million, versus previous guidance of \$18 million to \$21 million.

#### **Non-GAAP Financial Measures**

Ironwood 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, the amortization of acquired intangible assets, 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, and the impairment of intangible assets associated with Ironwood's subsequent notice of termination of the lesinurad license agreement. 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. Impairment of intangible assets is a non-cash charge that Ironwood considers to be non-recurring as it is associated with its notice of termination of the lesinurad franchise. As such, management believes that excluding the impairment of intangible assets provides more transparency into Ironwood's continuing operations. 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, November 6, 2018 to discuss its third 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 6878976. To access the webcast, please visit the Investors section of Ironwood's website at [www.ironwoodpharma.com](http://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 6, 2018 running through 11:59 p.m. Eastern Time on November 13, 2018. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 6878976. 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 discovered, developed and are commercializing linaclotide, the U.S. branded prescription market leader for adults with irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC). Our pipeline priorities for linaclotide include a Phase IIIb trial evaluating its efficacy and safety on multiple abdominal symptoms, including abdominal bloating, pain, and discomfort in adult patients with IBS-C, as well as research into a formulation of linaclotide designed to relieve pain across all IBS subtypes.

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 and sickle cell disease. Ironwood was founded in 1998 and is headquartered in Cambridge, Mass. For more information, please visit [www.ironwoodpharma.com](http://www.ironwoodpharma.com) or [www.twitter.com/ironwoodpharma](https://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 2.2 million unique patients have filled approximately 12.2 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 or CIC. 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 $\geq$ 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](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](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.inwdpi.com/duzallo/DuzalloPlandMedguide2017.pdf#page=1>

LINZESS® and CONSTELLA® are registered trademarks of Ironwood Pharmaceuticals, Inc., and ZURAMPIC® and DUZALLO® are registered trademarks of AstraZeneca AB. Any other trademarks referred to in this press release are the property of their respective owners. All rights reserved.

*This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including statements about the proposed separation of our operations into two independent, publicly traded companies, including the status, completion and timing of the separation; the business and operations of Ironwood and R&D Co. and any benefits or costs of the separation, including the tax treatment; the timing of effectiveness of the termination of the lesinurad license agreement and the transition of lesinurad operations; the financial profiles and capital structures of Ironwood and R&D Co.; expectations and timing regarding Ironwood's ability to achieve profitability; expectations regarding R&D Co.'s market, products, development and commercialization plans and ability to develop its pipeline; the development, launch, commercial availability and commercial potential of our products, product candidates and the other products that we promote and the drivers, timing, impact and results thereof; market size, commercial potential, prevalence, and the growth in, and potential demand for, our products and product candidates, as well as their potential impact on applicable markets; the potential indications for, and benefits of, our products and product candidates; the anticipated timing of preclinical, clinical and regulatory developments and the design, timing, size and results of clinical and preclinical studies; expected periods of patent exclusivity, durability and life of the patent portfolios for our products and product candidates; the strength of the intellectual property protection for our products and product candidates; and our financial performance and results, and guidance and expectations related thereto (including the drivers and timing thereof), including expectations related to the allocation of capital, LINZESS net price, LINZESS brand-specific adjustments, LINZESS U.S. net sales, ex-U.S. revenue (including API revenue), R&D, SG&A and marketing and sales expenses, net interest expense, total restructuring costs, the non-recurrence of impairment charges to intangible assets and plans to revise cash guidance. 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 possibility that we may not complete the separation of our business on the terms or timeline currently contemplated, if at all, achieve the expected benefits of the separation, and that the separation could harm our business, results of operations and financial condition; the risk that the transaction might not be tax-free; the risk that we may be unable to make, on a timely or cost-effective basis, the changes necessary to operate as independent companies; R&D Co.'s lack of independent operating history and the risk that its accounting and other management systems may not be prepared to meet the financial reporting and other requirements of operating as an independent public company; the risk that a separation may adversely impact our ability to attract or retain key personnel; the risk that we may experience difficulties in implementing or negative effects from the reduction in workforce, such as claims arising out of the reduction; risks related to the difficulty of predicting the financial impact or timing of our reduction in workforce; 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 our products and product candidates; decisions by regulatory and judicial authorities; the risk that we may never get sufficient patent protection for our products and 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, our products or 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, 2018, and in our subsequent SEC filings. These forward-looking statements (except as otherwise noted) speak only as of the date of this press release, and Ironwood undertakes no obligation to update these forward-looking statements. 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, December 31,	
	2018	2017
<b>Assets</b>		
Cash, cash equivalents and available-for-sale securities	\$ 161,398	\$ 221,416
Accounts receivable, net	65,375	82,157
Inventory, net	76	735
Prepaid expenses and other current assets	21,699	7,288
Total current assets	248,548	311,596
Restricted cash	7,676	7,056
Property and equipment, net	16,161	17,274
Convertible note hedges	142,774	108,188
Intangible assets, net	-	159,905

Goodwill	785	785
Other assets	708	870
Total assets	\$ 416,652	\$ 605,674
<b>Liabilities and Stockholders' (Deficit) Equity</b>		
Accounts payable, accrued expenses and other current liabilities	\$ 59,378	\$ 61,508
Capital lease obligations	171	4,077
Current portion of deferred rent	247	195
Current portion of long- term debt	39,191	-
Current portion of contingent consideration	74	247
Deferred revenue	13,521	-
Total current liabilities	112,582	66,027
Deferred rent, net of current portion	6,113	5,449
Other liabilities	2,530	5,060
Contingent consideration, net of current portion	-	31,011
Note hedge warrants	122,778	92,188
Convertible notes	261,355	249,193
Long-term debt	108,589	146,898
Total stockholders' (deficit) equity	(197,295)	9,848
<b>Total liabilities and stockholders' (deficit) equity</b>	<b>\$ 416,652</b>	<b>\$ 605,674</b>

### Condensed Consolidated Statements of Operations

(In thousands, except per share amounts)

(unaudited)

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2018	2017	2018	2017
Total revenues	\$65,686	\$86,825	\$215,947	\$ 204,068
Cost and expenses:				
Cost of revenues, excluding amortization of acquired intangible assets	4,616	6,080	11,288	10,113
Write-down of inventory to net realizable value and (settlement) loss on non-cancellable purchase commitments	(1,589)	71	247	167
Research and development	46,794	37,065	122,231	108,111
Selling, general and administrative	55,248	61,774	183,112	175,170
Amortization of acquired intangible assets	1,159	1,897	8,111	2,738
(Gain) loss on fair value remeasurement of contingent consideration	(33,519)	(628)	(31,045)	7,919
Restructuring expenses	10,282	-	15,096	-
Impairment of intangible assets	151,794	-	151,794	-
Total cost and expenses	234,785	106,259	460,834	304,218
Loss from operations	(169,099)	(19,434)	(244,887)	(100,150)
Other (expense) income:				
Interest expense, net	(8,741)	(8,534)	(25,984)	(25,672)
Gain (loss) on derivatives	3,489	(4,329)	3,996	(1,191)
Loss on extinguishment of debt	-	-	-	(2,009)
Other expense, net	(5,252)	(12,863)	(21,988)	(28,872)
GAAP net loss	\$(174,351)	\$(32,297)	\$(266,875)	\$ (129,022)
GAAP net loss per share—basic and diluted	\$(1.14)	\$(0.22)	\$(1.75)	\$(0.87)

Three Months Ended		Nine Months Ended	
September 30,		September 30,	
2018	2017	2018	2017

Non-GAAP net loss	\$(58,406)	\$(26,699)	\$(142,011)	\$(117,174)
Non-GAAP net loss per share (basic and diluted)	\$(0.38)	\$(0.18)	\$(0.93)	\$(0.79)
Weighted average number of common shares used in net loss per share — basic and diluted	153,227	149,502	152,143	148,695

### 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		Nine Months Ended,	
	September 30,		September 30,	
	2018	2017	2018	2017
GAAP net loss	\$(174,351)	\$(32,297)	\$(266,875)	\$(129,022)
Adjustments:				
Mark-to-market adjustments on the derivatives related to convertible notes, net	(3,489)	4,329	(3,996)	1,191
Amortization of intangible assets	1,159	1,897	8,111	2,738
Fair value remeasurement of contingent consideration	(33,519)	(628)	(31,045)	7,919
Impairment of intangible assets	151,794	-	151,794	-
Non-GAAP net loss	\$(58,406)	\$(26,699)	\$(142,011)	\$(117,174)

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

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2018	2017	2018	2017
GAAP net loss per share – Basic and Diluted	\$(1.14)	\$(0.22)	\$(1.75)	\$(0.87)
Adjustments to GAAP net loss per share (as detailed above)	0.76	0.04	0.82	0.08
Non-GAAP net loss per share – basic and diluted	\$(0.38)	\$(0.18)	\$(0.93)	\$(0.79)

### U.S. LINZESS Brand Collaboration<sup>1</sup>

#### Revenue/Expense Calculation

(In thousands)

(unaudited)

	Three Months Ended			
	September 30,			
	2018 excluding Net Sales Adjustment	Net Sales Adjustment <sup>2</sup>	2018	2017
LINZESS U.S. net sales	\$204,815	\$(59,326)	\$145,489	\$190,932
Commercial costs and expenses <sup>3</sup>	62,798	-	62,798	64,034

Commercial profit on sales of LINZESS	\$142,017	\$(59,326)	\$82,691	\$126,898
<i>Commercial Margin</i> <sup>4</sup>	69%		57%	66%
Ironwood's share of net profit			\$41,346	\$63,449
Ironwood's selling, general and administrative expenses <sup>5</sup>			10,915	10,456
Profit share adjustment			-	1,677
Ironwood's collaborative arrangement revenue			\$52,261	\$75,582

<sup>1</sup> 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, 2018, net profit for the U.S. LINZESS brand collaboration with Allergan was \$66.2 million, calculated by subtracting \$62.8 million in commercial costs and expenses and \$16.5 million in research and development expenses, from LINZESS U.S. net sales of \$145.5 million (which includes an approximately \$59.3 million negative adjustment to LINZESS net sales which was reported to Ironwood by Allergan). Net brand profit of \$66.2 million for the three months ended September 30, 2018, excluding the approximately \$59.3 million negative adjustment to LINZESS net sales, would have been \$125.5 million.

<sup>2</sup> During the three months ended September 30, 2018, Allergan reported to Ironwood an approximately \$59.3 million negative adjustment to LINZESS net sales. Such adjustment relates to the cumulative difference between certain previously estimated LINZESS gross-to-net sales reserves and allowances made by Allergan during the years ended December 31, 2015, 2016 and 2017, and actual subsequent payments made. This adjustment is primarily associated with estimated governmental and contractual rebates, as reported by Allergan. Upon receiving the information from Allergan, Ironwood recorded a \$29.7 million reduction to collaborative arrangement revenue and accounts receivable in its third quarter 2018 financial statements related to its share of the adjustment.

<sup>3</sup> 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.

<sup>4</sup> Commercial margin is defined as commercial profit on sales of LINZESS, as reported by Allergan, as a percent of total LINZESS U.S. net sales.

<sup>5</sup> Includes Ironwood's selling, general and administrative expenses attributable to the cost-sharing arrangement with Allergan.

## U.S. LINZESS Brand Collaboration<sup>1</sup>

### Revenue/Expense Calculation

(In thousands)

	Nine Months Ended			
	September 30,			
	2018 excluding Net Sales Adjustment	Net Sales Adjustment <sup>2</sup>	2018	2017
LINZESS U.S. net sales	\$555,975	\$(59,326)	\$496,649	\$506,380
Commercial costs and expenses <sup>3</sup>	198,411	-	198,411	215,174
Commercial profit on sales of LINZESS	\$357,564	\$(59,326)	\$298,238	\$291,206
<i>Commercial Margin</i> <sup>4</sup>	64%		60%	58%
Ironwood's share of net profit			\$149,119	\$145,603
Ironwood's selling, general and administrative expenses <sup>5</sup>			33,556	34,061
Profit share adjustment			-	1,677
Ironwood's collaborative arrangement revenue			\$182,675	\$181,341

<sup>1</sup> 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.

<sup>2</sup> During the three months ended September 30, 2018, Allergan reported to Ironwood an approximately \$59.3 million negative adjustment to LINZESS net sales. Such adjustment relates to the cumulative difference between certain previously estimated LINZESS gross-to-net sales reserves and allowances made by Allergan during the years ended December 31, 2015, 2016 and 2017, and actual subsequent payments made. This adjustment is primarily associated with estimated governmental and contractual rebates, as reported by Allergan. Upon receiving the information from Allergan, Ironwood recorded a \$29.7 million reduction to collaborative arrangement revenue and accounts receivable in its third quarter 2018 financial statements related to its share of the adjustment.

<sup>3</sup> 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.

<sup>4</sup> Commercial margin is defined as commercial profit on sales of LINZESS, as reported by Allergan, as a percent of total LINZESS U.S. net sales.

<sup>5</sup> Includes Ironwood's selling, general and administrative expenses attributable to the cost-sharing arrangement with Allergan.

View source version on businesswire.com: <https://www.businesswire.com/news/home/20181106005528/en/>

Source: Ironwood Pharmaceuticals, Inc.

Ironwood Pharmaceuticals, Inc.  
Meredith Kaya, 617-374-5082  
Vice President, Investor Relations and Corporate Communications  
[mkaya@ironwoodpharma.com](mailto:mkaya@ironwoodpharma.com)