Ironwood Pharmaceuticals

A Leading GI Healthcare Company

NASDAQ: IRWD





Safe Harbor Statement

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Investors are cautioned not to place undue reliance on these forward-looking statements, including statements about our ability to execute on our mission; our strategy, business, financial position and operations, including with respect to our strategic priorities; the demand, development, commercial availability and commercial potential of linaclotide and the drivers, timing, impact and results thereof; the potential indications for, and benefits of, linaclotide and our ability to drive LINZESS growth; expectations regarding our financial performance and results, and guidance and expectations related thereto, including, without limitation expectations related to LINZESS prescription demand growth, LINZESS U.S. net sales, Ironwood revenue and adjusted EBITDA in 2024; the assessment of the data from the Phase III STARS clinical trial of apraglutide; the efficacy and safety of apraglutide; the timing of topline data for CNP-104, which will inform a decision on our option to acquire an exclusive license from COUR, and that, if successful, CNP-104 has the potential to be a disease-modifying therapy for PBC; the progress of ongoing clinical trials and the timing of related data readouts. These forward-looking statements speak only as of the date of this presentation, and Ironwood undertakes no obligation to update these forward-looking statements. 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 of linaclotide, apraglutide, CNP-104, IW-3300, and other product candidates; the risk that clinical programs and studies, inducing for the linaclotide pediatric program, apraglutide, CNP-104 and IW-3300, may not progress or develop as anticipated, including that studies are delayed or discontinued for any reason, such as safety, tolerability, enrollment, manufacturing, economic or other reasons; the risk that findings from our completed nonclinical studies and clinical trials may not be replicated in later trials and earlier-stage clinical trials may not be predictive of the results we may obtain in later-stage clinical trials or of the likelihood of regulatory approval; the risk of competition or that new products may emerge that provide different or better alternatives for treatment of the conditions that our products are approved to treat; the risk that we are unable to execute on our strategy to in-license externally developed products or product candidates; the risk that we are unable to successfully partner with other companies to develop and commercialize products or product candidates; the risk that healthcare reform and other governmental and private payor initiatives may have an adverse effect upon or prevent our products' or product candidates' commercial success; the efficacy, safety and tolerability of linaclotide and our product candidates; the risk that the commercial and therapeutic opportunities for LINZESS, apraglutide, or our product candidates are not as we expect; decisions by regulatory and judicial authorities; the risk that we may never get additional patent protection for linaclotide, apraglutide, and other product candidates, that patents for linaclotide, apraglutide, or other products may not provide adequate protection from competition, or that we are not able to successfully protect such patents; the risk that we are unable to manage our expenses or cash use, or are unable to commercialize our products as expected; the risk that the development of the linaclotide pediatric program, apraglutide, CNP-104 and/or IW-3300 are not successful or that any of our product candidates is not successfully commercialized; outcomes in legal proceedings to protect or enforce the patents relating to our products and product candidates, including abbreviated new drug application; the risk that financial and operating results may differ from our projections; 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; developments in accounting guidance or practice; Ironwood's or AbbVie's accounting practices, including reporting and settlement practices as between Ironwood and AbbVie; the risk that we are unable to manage our expenses or cash use, or are unable to commercialize our products 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, 2023, and in our subsequent SEC filings.

Ironwood uses non-GAAP financial measures in this presentation, which should be considered only a supplement to, and not a substitute for or superior to, GAAP measures. Refer to the Reconciliation of Non-GAAP Financial Measures to GAAP Results table and to the Reconciliation of Adjusted EBITDA to GAAP net loss table and related footnotes on pages 42 to 44 of this presentation. Further, Ironwood considers the net profit for the U.S. LINZESS brand collaboration with AbbVie in assessing the product's performance and calculates it based on inputs from both Ironwood and AbbVie. 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 on pages 45 to 46 of this presentation.

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Our vision is to be the leading
GI healthcare company focused on advancing
the treatment of GI diseases and redefining the
standard of care for GI patients

Leading the Way in GI Innovation

Ironwood is uniquely positioned to drive value as a GI-focused biotech with strong LINZESS cash flows expected until generic entry in 2029

OUR FOCUSED PRIORITIES:



Maximize LINZESS



Advance GI pipeline Highlighted by apraglutide for SBS-IF1 and CNP-104 for PBC2



Deliver sustained profits & cash flow

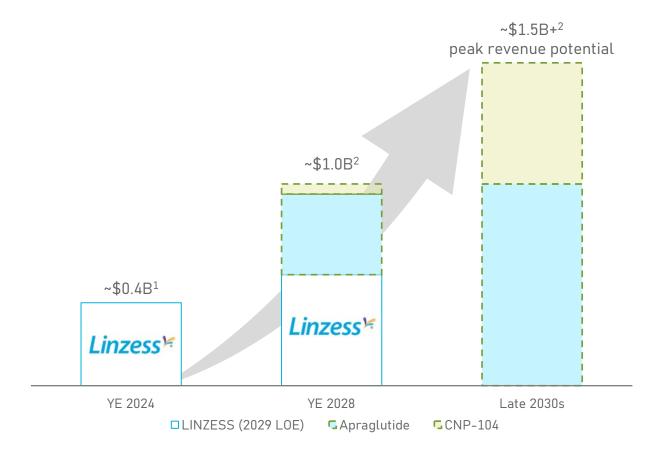


\$1.5B+ Revenue Potential through the 2030s

Apraglutide and CNP-104 have the potential to extend growth through the 2030s and drive value for patients and shareholders

Ironwood Today (LINZESS)

Pro Forma Ironwood Long Term (Assuming apraglutide and CNP-104 approval)





¹ Reflects guidance for 2024 Ironwood collaborative arrangement revenue from LINZESS

² Ironwood management estimate, not risk-adjusted

We have an exciting GI pipeline highlighted by apraglutide for adult patients with SBS dependent on PS and CNP-104 for PBC







LINZESS

The U.S. prescription market leader for adults with Irritable Bowel Syndrome with Constipation (IBS-C) and Chronic Idiopathic Constipation (CIC)

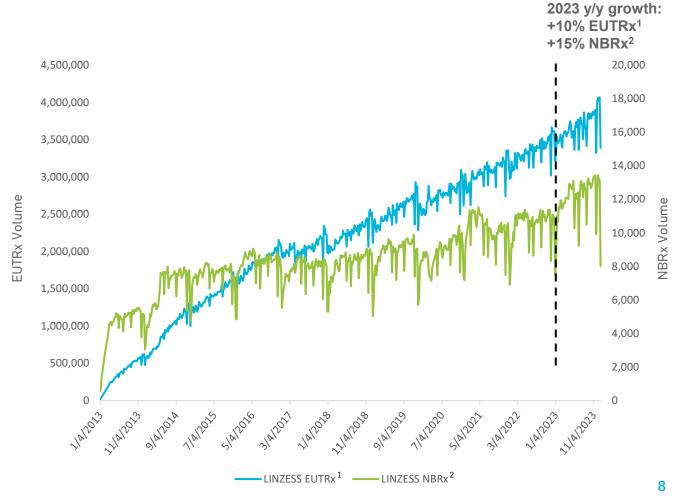


Leader in IBS-C and CIC

LINZESS is a growing, market leading, blockbuster brand with a significant opportunity to address high unmet need



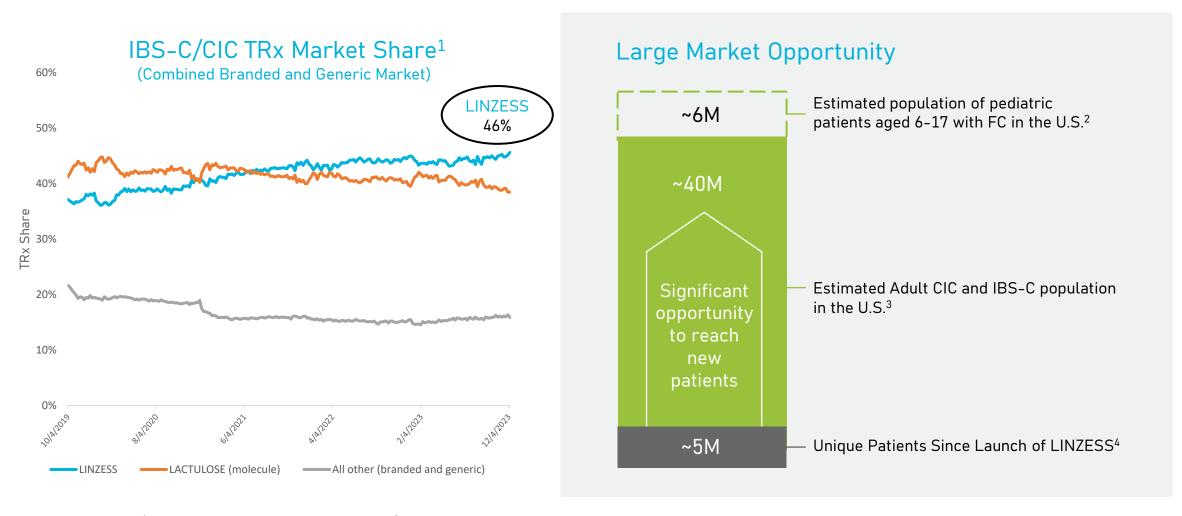
Impressive LINZESS Demand Growth Since Launch



Ironwood

 $^{^1}$ EUTRx, total prescription extended units; IQVIA Weekly National Prescription Audit 2 NBRx, new-to-brand prescriptions prescriptions; IQVIA Weekly Patients Insights

LINZESS is the prescription market leader in the U.S. for adults with IBS-C/CIC with a large market opportunity







First and only FDA approved Rx therapy to treat pediatric functional constipation for patients ages 6-17

Significant unmet patient need and opportunity

- Commercially available as of June 2023 with existing 72 mcg dose for patients aged 6-17 years-old; benefits from existing LINZESS class-leading payer access
- Highly symptomatic condition with patients actively seeking care due to distressing symptoms
- Efficient investment planned to realize opportunity



Apraglutide

Glucagon-like peptide 2 (GLP-2) analog for adult patients with short bowel syndrome who are dependent on parenteral support



Apraglutide advances Ironwood's GI leadership and creates value for patients and shareholders

Apraglutide has the potential to establish a new standard of care for adult patients with SBS who are dependent on PS and achieve blockbuster status, if approved



 Apraglutide's Phase III results support potential to be the only once weekly GLP-2 for the whole spectrum of adult patients with SBS who are dependent on PS



Leverages Ironwood's GI capabilities and success with LIN7FSS



- \$1B+ Apraglutide peak net sales potential²
- Potential to enhance Ironwood's long-term financial profile through the 2030s



¹ Agraglutide has not been proven effective or safe for its intended use and there is no guarantee that it will receive regulatory approval to commercialize

² Ironwood management estimate, not risk-adjusted

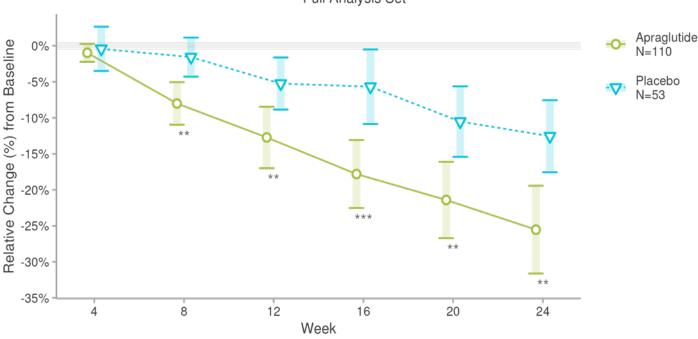


Primary Endpoint

Apraglutide met its primary endpoint of relative change from baseline in actual weekly parenteral support volume at week 24, a 2x treatment effect relative to placebo, driven by both stoma and colon-in-continuity populations

Primary Analysis of Relative Change (%) from Baseline in Actual Parenteral Support Weekly Volume

Full Analysis Set



Missing data are imputed using the placebo-based method. Data points represent the least square means and its 95% confidence interval using Rubin's rule to combine results from multiple imputation data sets, analyzed by mixed-effect model repeated measurements (MMRM).

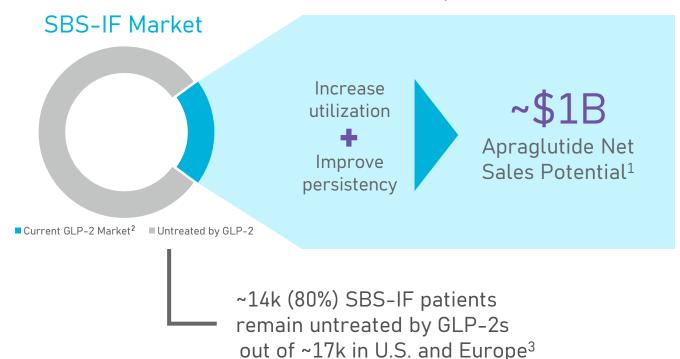
* p<0.05; ** p<0.01, *** p<0.001.



Apraglutide has potential to achieve ~\$1B in peak net sales¹

Apraglutide target product profile can enable market leadership position in adult patients with SBS who are dependent on parenteral support

Apraglutide target product profile has the potential to:





¹ Ironwood management estimate, not risk-adjusted, if successfully developed and approved ² Gattex estimated 2023 net sales of ~\$750 million

³ Komodo Health claims data analysis (US), 2022; IQVIA MIDAS data analysis (EU), 2022

STARS Phase 3 data reinforce apraglutide's potential to improve the standard of care for SBS patients dependent on parenteral support (PS)

Once-Weekly Efficacy

- Apraglutide is the only GLP-2 analog to achieve significant reduction vs. placebo in weekly PS volume relative to baseline at Week 24 with onceweekly dosing
- Rapid onset of treatment effect by week 8 and onward
- Treatment effect similar across most predefined subgroups

Days Off PS and Enteral Autonomy

- PS volume reduction with significantly more apraglutidetreated patients achieving additional ≥1, ≥ 2 and ≥3 days off PS per week
- 7 patients achieved enteral autonomy by Week 24, including both stoma and colon-in-continuity patients vs. 0 patients on placebo

Safety and Tolerability

- Apraglutide demonstrated high rates of compliance in Phase 3 study
- Incidence of treatment-related AEs and SAEs was comparable between treatment arms with no malignancies
- No patients discontinued from treatment due to GI tolerability symptoms, GI obstructions, GI polyps or neoplasms





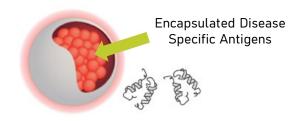
CNP-104

Potential disease-modifying therapy for the treatment of Primary Biliary Cholangitis (PBC)



CNP-104: a potentially new game-changing therapy for PBC patients

COUR's proprietary platform combines PDC-E2 with state-of-the-art pharmaceutical nanoparticles to tolerize the immune system and potentially eliminate the immune cell bile duct destruction present in PBC



Proprietary PLGA nanoparticle with PDC-E2 encapsulated

PDC-E2 Antigen

Well-characterized and common PBC autoantigen: PDC-E2 protein

 T cell dependent autoimmune mechanisms drive PBC disease pathology

Nanoparticle Platform

- COUR's platform has shown clinical proof of technology in other antigen specific autoimmune diseases
- Scientifically established nanoparticle platform

PBC affects an estimated 130K patients in the U.S.¹

CNP-104 has the potential to be the first PBC disease-modifying therapy

CNP-104 targets the root cause of PBC; there are no therapies on the market today that address the root cause of the autoimmune destruction of the bile ducts

Initial assessment provided evidence of favorable T-cell response in patients dosed with CNP-104

Ironwood maintains an option to exclusively license CNP-104 for continued development pending proof of concept and commercial viability



CNP-104: Phase 2 proof of concept study in Primary Biliary Cholangitis (PBC)

Expect topline data in Q3 2024

CNP-104 has the potential to be a disease-modifying therapy for PBC

42 patients with PBC

Randomized, Double-blinded, placebo-controlled, parallel assignment

Doses:

Placebo, CNP-104 4mg/kg, CNP-104 8mg/kg

IV Infusion on Days 1 and 8

STUDY OBJECTIVES

Safety, tolerability, pharmacodynamics (PD), and efficacy of two doses of CNP-104

KEY OUTCOMES:

Placebo

- Immunological endpoints (e.g. T-cell response)
- Markers of liver function

CNP-104 (4mg/kg)

CNP-104 (8mg/kg)

20 month Long-Term Safety and Durability

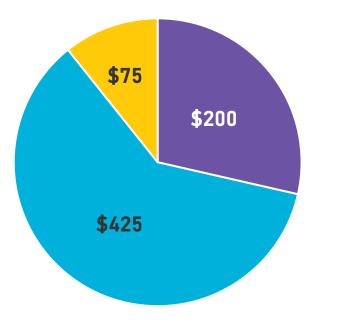


Financials

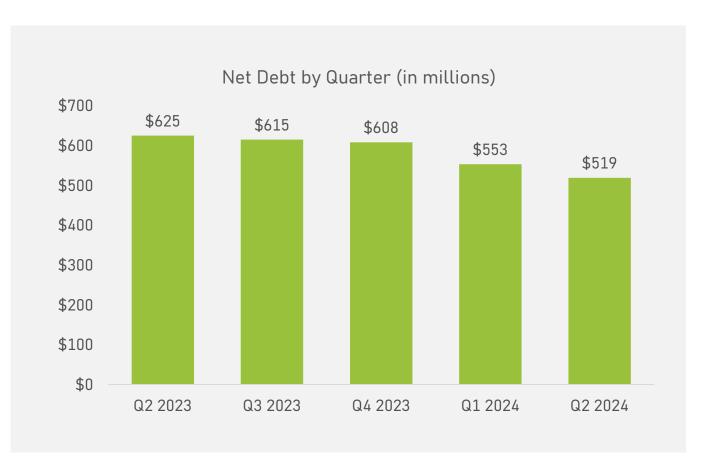
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Strong LINZESS cash flows enable rapid de-levering while simultaneously funding on-going operations across portfolio to drive long-term growth









\$106 million in cash & cash equivalents as of June 30, 2024



Revised FY 2024 guidance reflects continued LINZESS pricing pressure as a result of higher-than-expected Medicaid utilization trends

Ironwood®	Previous FY 2024 Guidance (May 9, 2024)	Revised FY 2024 Guidance (August 8, 2024)
LINZESS U.S. net sales	Mid-single digits % decline ²	\$900 – \$950 million
Ironwood revenue	\$405 – \$425 million	\$350 – \$375 million
Adjusted EBITDA ¹	>\$120 million Excludes potential CNP-104 option exercise	>\$75 million Excludes potential CNP-104 option exercise



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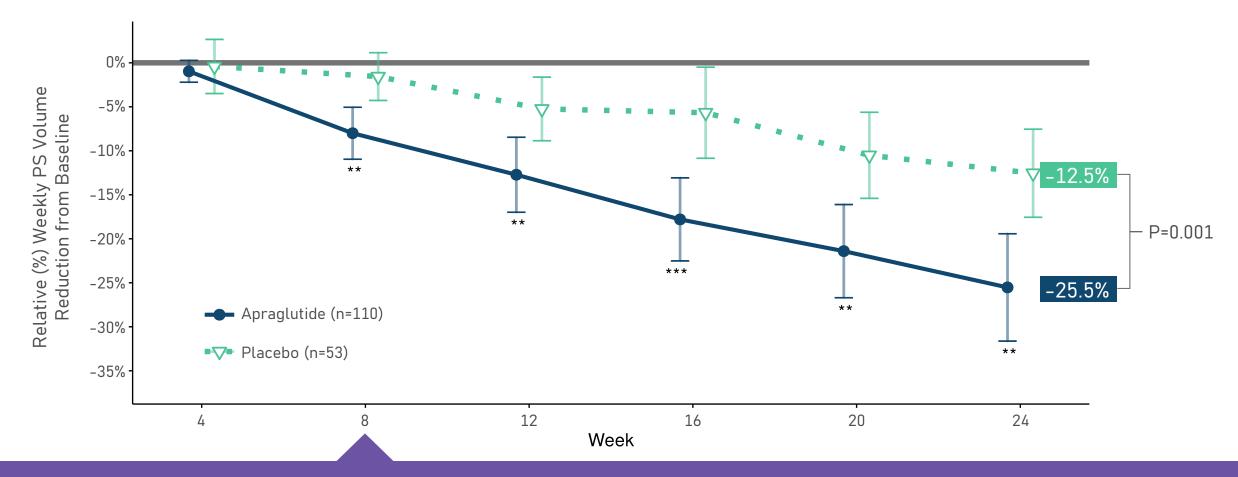


Appendix

Apraglutide SBS-IF



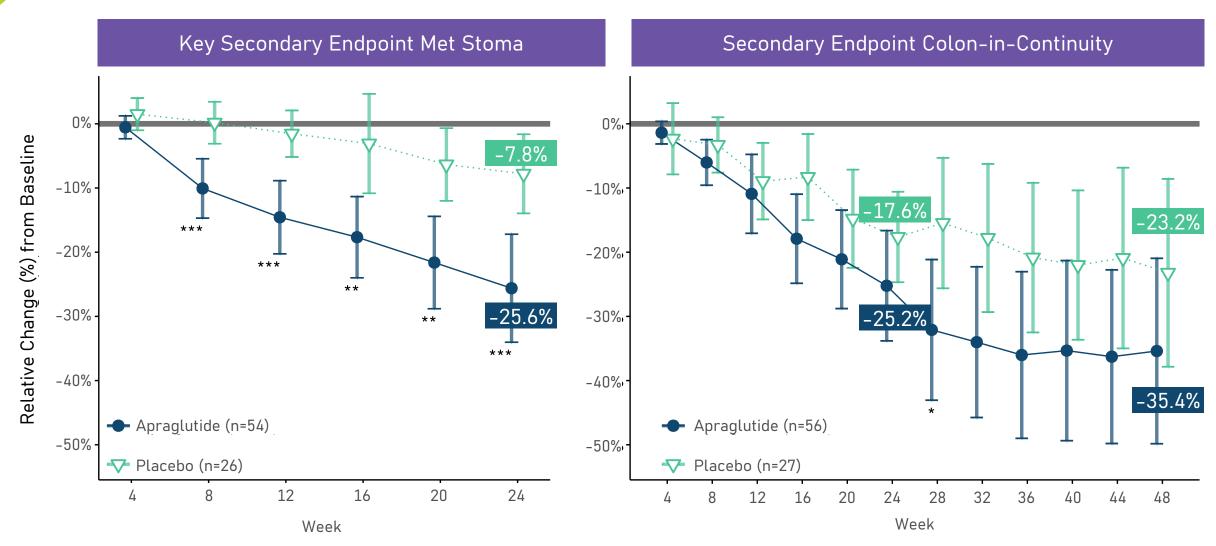
Primary endpoint met (overall population): significantly greater relative reduction in weekly PS volume at Week 24



Apraglutide treatment effect observed at Week 8 and onward



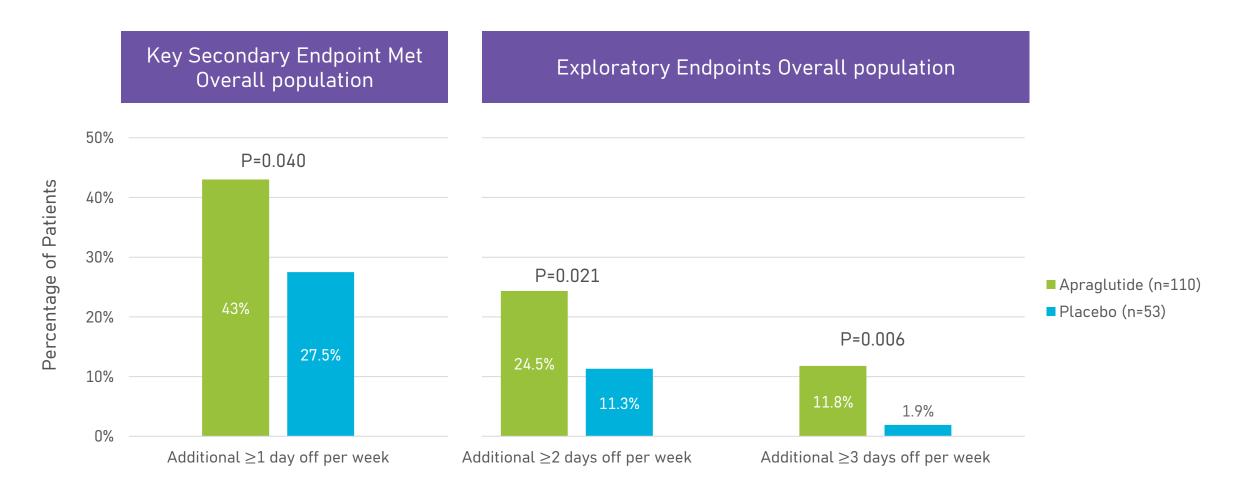
Both stoma and colon-in-continuity contributed to meeting the primary endpoint





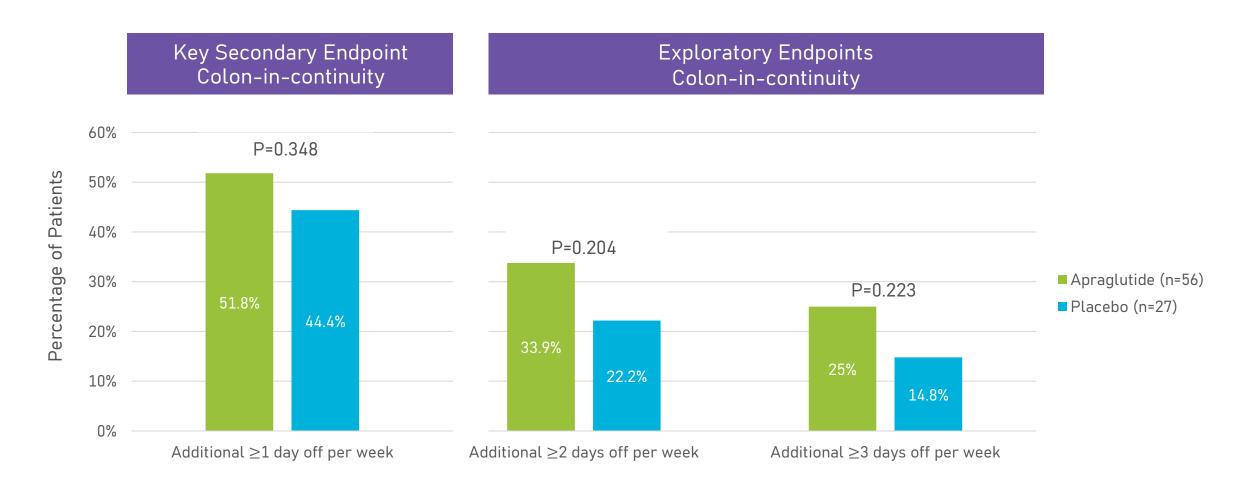
p<0.05; **p<0.01; ***p<0.001;

Significantly more apraglutide-treated patients in the overall population gained additional ≥ 2 and ≥ 3 days off PS per week at Week 24



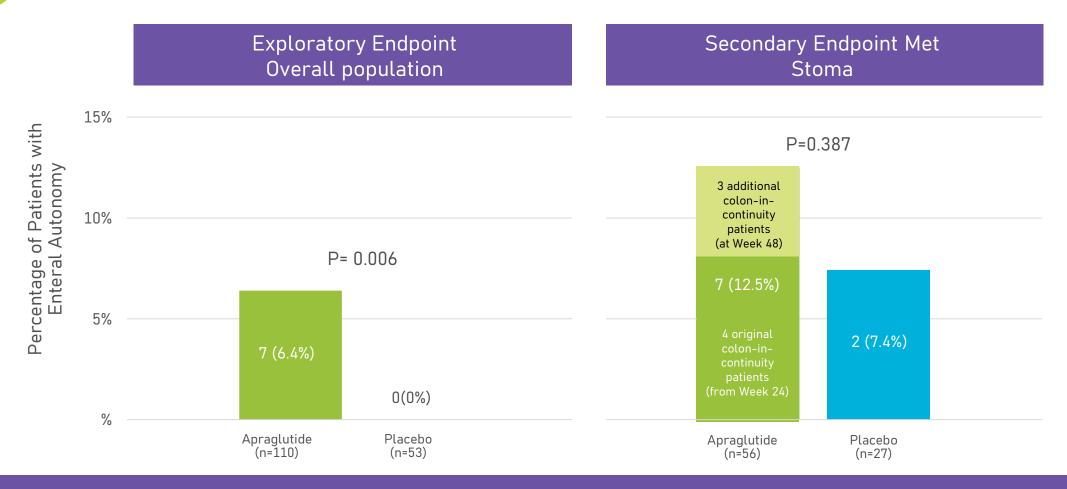


Numerically more apraglutide-treated colon-in-continuity patients gained additional ≥ 2 and ≥ 3 days off PS per week at Week 48





Proportion of apraglutide-treated patients achieving enteral autonomy

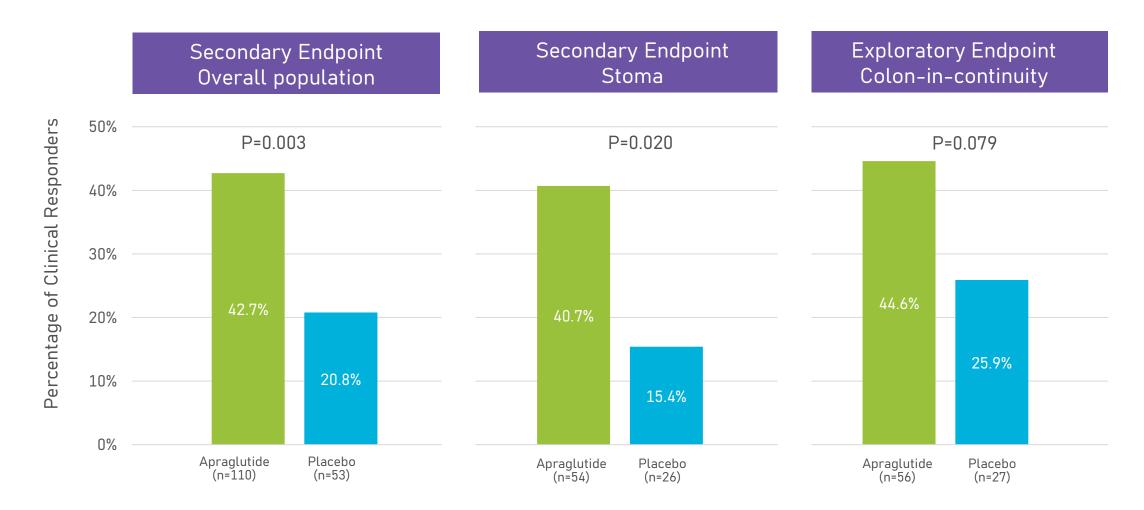


All 4 colon-in-continuity patients who achieved enteral autonomy at Week 24 remained off PS at Week 48

The 3 patients with stoma maintained enteral autonomy 48 weeks after randomization



Proportion of clinical responders in stoma & colon-in-continuity patients (≥20% PS volume reduction at both Weeks 20 and 24)





Secondary endpoint (stoma): significantly more apraglutide-treated patients were clinical high responders (\geq 40% PS volume reduction at both Weeks 20 and 24)





Safety & tolerability: apraglutide was well tolerated with few discontinuations due to adverse events

Incidence of AEs & SAEs through Week 48 in the Overall Population

	Apraglutide (n=110)	Placebo (n=53)
AE	99 (90.0)	47 (88.7)
AE leading to dose reduction	0 (0.0)	0 (0.0)
AE leading to dose interruption	12 (10.9)	6 (11.3)
AE leading to discontinuation	4 (3.6)	1 (1.9)
Treatment-related AE	39 (35.5)	23 (43.4)
SAE	39 (35.5)	17 (32.1)
Treatment-related SAE	3 (2.7)	3 (5.7)

- Incidence of treatment-related AEs and SAEs was comparable between treatment arms
- One fatal SAE was reported in apraglutide arm and assessed as unrelated
- No patients discontinued from treatment due to GI tolerability symptoms, GI obstructions, GI polyps or neoplasms
- Incidence of GI polyps:
 - Apraglutide: 3 events (n=3; 2.7%)
 - Placebo: 3 events (n=2; 3.8%)



Safety & tolerability: safety profile is consistent with previous apraglutide clinical studies

Most Frequent AEs t hrough Week 48		
Preferred Terms	Apraglutide (n=110) n (%)	Placebo (n=53) n (%)
Nausea	15 (13.6)	6 (11.3)
Vascular device infection	14 (12.7)	5 (9.4)
Headache	14 (12.7)	6 (11.3)
Abdominal pain	12 (10.9)	5 (9.4)
Diarrhea	11 (10.0)	5 (9.4)
Fatigue	11 (10.0)	3 (5.7)
Nasopharyngitis	10 (9.1)	2 (3.8)
Abdominal distension	9 (8.2)	4 (7.5)
Arthralgia	8 (7.3)	5 (9.4)

- Relatively low incidence of AEs associated with GI tolerability between treatment arms
- Incidence of injection site reaction*
 was reported in 10 (9.1%) apraglutide-treated
 patients vs. 4 (7.5%) patients with placebo
- No malignancy was reported during the study



^{*} Injection site reaction is a grouped term that included preferred terms such as injection site pain, injection site pruritus, injection site erythema, injection site edema, and injection site bruising



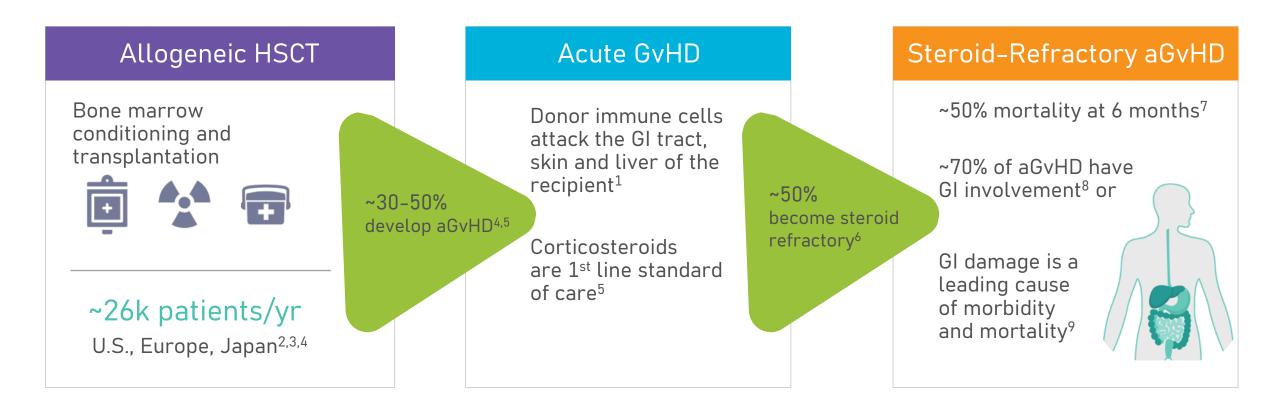
Appendix

Apraglutide GvHD



Acute GvHD is a life-threatening condition resulting from allogeneic hematopoietic stem cell transplant (HSCT)¹

Significant unmet need for non-immunosuppressive treatments with greater efficacy and durability





First-In-Class Phase 2 exploratory study in graft vs. host disease (GvHD)

Positive data announced in Q1 2024

The primary findings add to the body of evidence about the safety and tolerability of apraglutide



Patients with steroid-refractory acute GI GvHD in combination with systemic steroids (SS) + ruxolitinib (rux)

up to 34 patients

>12 years and older

Blinded to dose, externally-controlled

STUDY OBJECTIVES

Safety and tolerability; PK; efficacy measures including response rate, duration of response, survival-related outcomes

Up to 90 days treatment

Weekly Dose Level 1 Apraglutide + SS/rux

Weekly Dose Level 2 Apraglutide + SS/rux

External control

Follow up to 2 years

All lower GI responders at Day 28 maintained their response through days 56 and 91





Appendix

IW-3300

Ironwood°

IW-3300: Phase 2 Proof of Concept Study in IC/BPS

Opportunity to test "cross-talk" hypothesis in humans for the first time

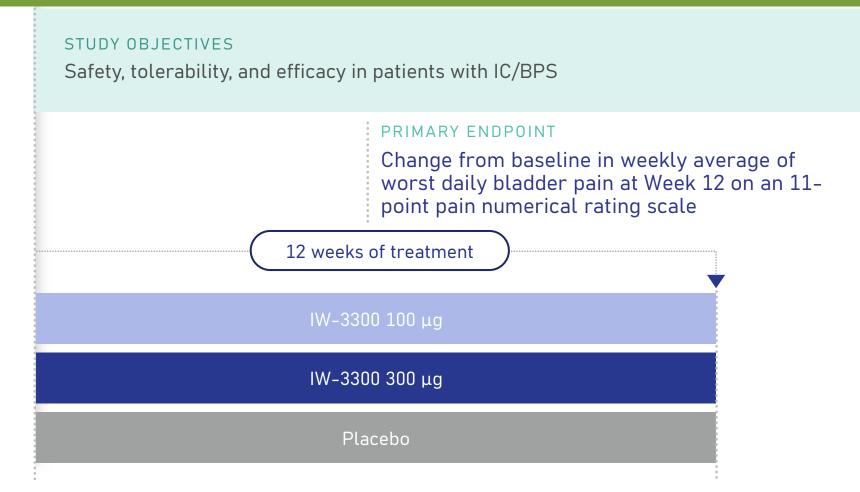
300 patients with Interstitial Cystitis / Bladder Pain Syndrome (IC/BPS)

Randomized, double-blinded, placebo-controlled, parallel assignment

Doses:

Placebo, IW-3300 100 μg, IW-3300 300 μg

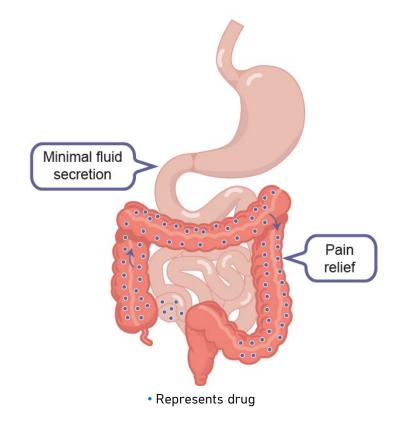
Rectal foam administered daily to provide adequate target tissue engagement and exposure





IW-3300: GC-C Agonist For Visceral Pain Conditions

- Strong pre-clinical evidence combined with sound scientific & commercial rationale supports POC study to explore potential impact of IW-3300 on chronic visceral pain outside of GI tract
- Strong pre-clinical data:
 - IW-3300 demonstrated pain relief in bladder pre-clinical hypersensitivity model
 - IW-3300 reversed endometriosis-induced vaginal hypersensitivity in a pre-clinical vaginal distension model
- Very high unmet need in Interstitial Cystitis / Bladder Pain Syndrome (IC/BPS) and in Endometriosis
 - · Limited number of treatment options available
 - Patients surveyed report experiencing a low QoL and many reported experiencing reduced productivity
- Ironwood is continuing the Phase II proof of concept study in IC/BPS and actively evaluating partnership options



Target indications are strategically linked to GC-C mechanism and supportive preclinical data, designed to address a significant medical need and have a defined path to POC





Appendix

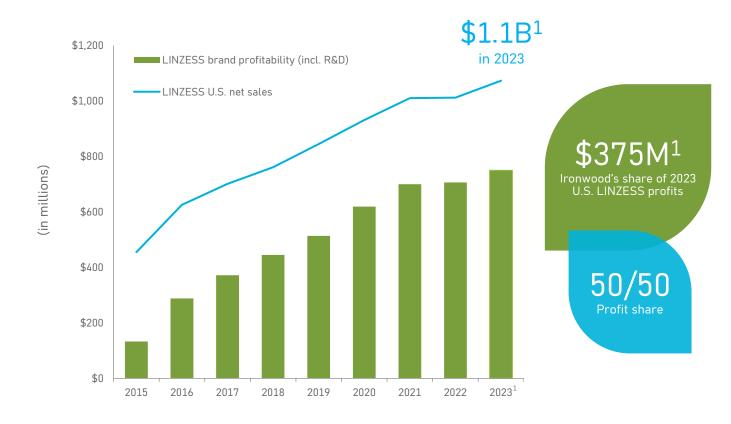
LINZESS



LINZESS continues to generate strong brand profits

LINZESS demand is increasing and fueling U.S. net sales and brand profitability







¹ LINZESS U.S. net sales and brand profitability and Ironwood's share of U.S. LINZESS profits reflects our FY 2023 results. LINZESS net sales are recognized using AbbVie's revenue recognition accounting policies and reporting conventions. As a result, certain rebates and discounts are classified as LINZESS U.S. commercial costs, expenses and other discounts within Ironwood's calculation of collaborative arrangements revenue. LINZESS costs include certain discounts recognized and cost of goods sold incurred by AbbVie; also includes commercial costs incurred by AbbVie and Ironwood that are attributable to the cost-sharing arrangement between the parties. See slide 45 for detailed breakdown.

Appendix

Financials

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Reconciliation of GAAP results to non-GAAP financial measures (page 1)

	Three Months Ended June 30, 2024	Six Months Ended June 30, 2024
	(000s, except per share amounts)	(000s, except per share amounts)
GAAP net loss ^{1,2}	(860)	(5,022)
Adjustments:		
Mark-to-market adjustments on the derivatives related to convertible notes, net	-	-
Amortization of acquired intangible assets	204	409
Restructuring expenses	2,067	2,504
Acquisition-related costs	359	1,146
Tax effect of adjustments	(262)	(461)
Non-GAAP net income (loss) ^{1,2}	1,508	(1,424)
GAAP net loss attributable to Ironwood per share – basic	(0.01)	(0.03)
Plus: GAAP net income (loss) attributable to noncontrolling interests – basic	-	-
Adjustments to GAAP net income (loss) (detailed above)	0.01	0.02
Non-GAAP net income (loss) per share – basic	-	(0.01)

¹ The company presents non-GAAP net income (loss) and non-GAAP net income (loss) per share to exclude the impact of net gains and losses on the derivatives related to our 2022 convertible notes that are required to be marked-to-market. 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. For a reconciliation of the company's non-GAAP financial measures to the most comparable GAAP measures, please refer to the table above. Additional information regarding the non-GAAP financial measures is included in the company's press release dated August 8, 2024. 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. In addition, these non-GAAP financial measures are unlikely to be comparable with non-GAAP information provided by other companies ² Figures presented for the three and six months ended June 30, 2024 include a \$17.0 million increase and \$13.0 million reduction to collaborative arrangement revenues, respectively, as a result of an adjustment recorded for Ironwood's estimate of LINZESS gross-to-net reserves as of June 30, 2024.

Reconciliation of GAAP results to non-GAAP financial measures (page 2)

	Three Months Ended June 30, 2024	Six Months Ended June 30, 2024
	(000s, except per share amounts)	(000s, except per share amounts)
GAAP net loss attributable to Ironwood per share – diluted	(0.01)	(0.03)
Plus: GAAP net income (loss) attributable to noncontrolling interests – diluted	-	-
Adjustments to GAAP net income (loss) (detailed above)	0.01	0.02
Non-GAAP net income (loss) per share – diluted	-	(0.01)

Reconciliation of GAAP net loss to adjusted EBITDA

	Three Months Ended June 30, 2024	Six Months Ended June 30, 2024
	(000s)	(000s)
GAAP net loss ^{1,2}	(860)	(5,022)
Adjustments:		
Mark-to-market adjustments on the derivatives related to convertible notes, net	-	-
Restructuring expenses	2,067	2,504
Interest expense	7,470	14,701
Interest and investment income	(1,369)	(2,538)
Income tax expense	19,736	28,856
Depreciation and amortization	506	1,019
Acquisition-related costs	359	1,146
Adjusted EBITDA ^{1,2}	27,909	40,666

¹Ironwood presents GAAP net income (loss) and adjusted EBITDA, a non-GAAP measure. Adjusted EBITDA is calculated by subtracting mark-to-market adjustments on derivatives related to Ironwood's 2022 Convertible Notes, restructuring expenses, interest expense, intere

LINZESS U.S. Brand Collaboration

Commercial Profit & Collaboration Revenue¹

	Three Months Ended June 30, 2024	Six Months Ended June 30, 2024
	(000s)	(000s)
LINZESS U.S. net product sales as reported by AbbVie ²	211,183	467,783
AbbVie & Ironwood commercial costs, expenses and other discounts ³	80,950	154,312
Commercial profit on sales of LINZESS	130,233	313,471
Commercial Margin ⁴	62%	67%
Ironwood's share of net profit	65,117	156,736
Reimbursement for Ironwood's commercial expenses	9,298	19,394
Adjustment for Ironwood's estimate of LINZESS gross-to-net reserves	17,000	(13,000)
Ironwood's U.S. collaboration revenue ⁵	91,415	163,130

¹ Ironwood collaborates with AbbVie 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 profit and bears 50% of the net

LINZESS U.S. Brand Collaboration

Ironwood & AbbVie Total Net Profit¹

	Three Months Ended June 30, 2024	Six Months Ended June 30, 2024
	(000s)	(000s)
LINZESS U.S. net product sales as reported by AbbVie ²	211,183	467,783
AbbVie & Ironwood commercial costs, expenses and other discounts ³	80,950	154,312
AbbVie & Ironwood R&D expenses ⁴	9,736	17,372
Total net profit on sales of LINZESS	120,497	296,099

¹ Ironwood collaborates with AbbVie 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., including the commercial costs and expenses and the research and development expenses related to LINZESS in the U.S. that are shared equally between the parties under the collaboration agreement. ² LINZESS net sales are recognized using AbbVie's revenue recognition accounting policies and reporting conventions. As a result, certain rebates and discounts are classified as LINZESS U.S. commercial costs, expenses and other discounts within Ironwood's calculation of collaborative arrangements revenue. ³ Includes certain discounts recognized and cost of goods sold incurred by AbbVie; also includes commercial costs incurred by AbbVie and Ironwood that are attributable to the cost-sharing arrangement between the parties. ⁴ R&D Expenses related to LINZESS in the U.S. are shared equally between Ironwood and AbbVie under the collaboration agreement.