A COMMERCIAL BIOTECHNOLOGY COMPANY

Barclays Healthcare Conference

March, 15 2018

Safe Harbor Statement

This presentation contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including statements about the development, launch, commercial availability and commercial potential of linaclotide, lesinurad, our product candidates and the other products that we promote and the drivers, timing, impact and results thereof; market size, prevalence, growth and opportunity, including peak sales (and drivers thereof) and the growth in and potential demand for linaclotide, lesinurad and our product candidates, as well as their potential impact on applicable markets; the potential indications for, and benefits of, linaclotide, lesinurad and our product candidates; the anticipated timing of preclinical, clinical and regulatory developments (including strengthening the clinical profile and expanding the clinical utility of linaclotide) and the design, timing and results of clinical and preclinical studies; the potential for, and timing of, regulatory submissions and approvals for linaclotide, lesinurad and our product candidates; partnering strategy; expected periods of patent exclusivity, durability and life of the respective patent portfolios for linaclotide, lesinurad and our product candidates; commercial strategy, including with respect to DUZALLO; the strength and durability of the intellectual property protection for linaclotide, lesinurad and our product candidates and our intentions and efforts to protect such intellectual property; and our financial performance and results, and guidance and expectations related thereto (including the drivers and timing thereof), including expectations related to a rapidly growing top-line, the exercise of financial discipline, maximizing long-term per-share cash flows for shareholders, Ironwood revenue CAGR and revenue growth, positive cash flow and positive cash flow from operations, LINZESS U.S. net sales, commercial margin, ex-U.S. revenue (including API revenue), and allocation of capital. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include those related to the effectiveness of development and commercialization efforts by us and our partners; preclinical and clinical development, manufacturing and formulation development; the risk that findings from our completed nonclinical and clinical studies may not be replicated in later studies; efficacy, safety and tolerability of linaclotide, lesinurad and our product candidates; decisions by regulatory and judicial authorities; the risk that we are unable to successfully integrate lesinurad into our existing business, commercialize lesinurad or realize the anticipated benefits of the lesinurad transaction; the risk that we may never get sufficient patent protection for linaclotide, lesinurad and our product candidates or that we are not able to successfully protect such patents; the outcomes in legal proceedings to protect or enforce the patents relating to our products and product candidates, including ANDA litigation; developments in the intellectual property landscape; challenges from and rights of competitors or potential competitors; the risk that our planned investments do not have the anticipated effect on our company revenues, linaclotide, lesinurad or our product candidates; the risk that we are unable to manage our operating expenses or cash use for operations, or are unable to commercialize our products, within the guided ranges or otherwise as expected; and the risks listed under the heading "Risk Factors" and elsewhere in Ironwood's 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 presentation, 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 our fourth quarter investor update press release dated February 15, 2018.

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What to expect in 2018

1

Rapidly growing top-line

U.S. LINZESS® (linaclotide)
Ex-U.S. LINZESS/CONSTELLA® (linaclotide)
DUZALLO® (lesinurad and allopurinol) **launch year**

>25% Ironwood revenue CAGR 2016-2020[1,2]

2

Decisively advancing late-stage candidates

2 Phase III programs initiating

≥4 Phase II trials ongoing

Active partnering discussions for IW-3718 and for praliciguat (IW-1973)

3

Exercising financial discipline

Positive cash flow in 4Q 2018[2]

Positive cash flow from operations in FY 2019[2,3]

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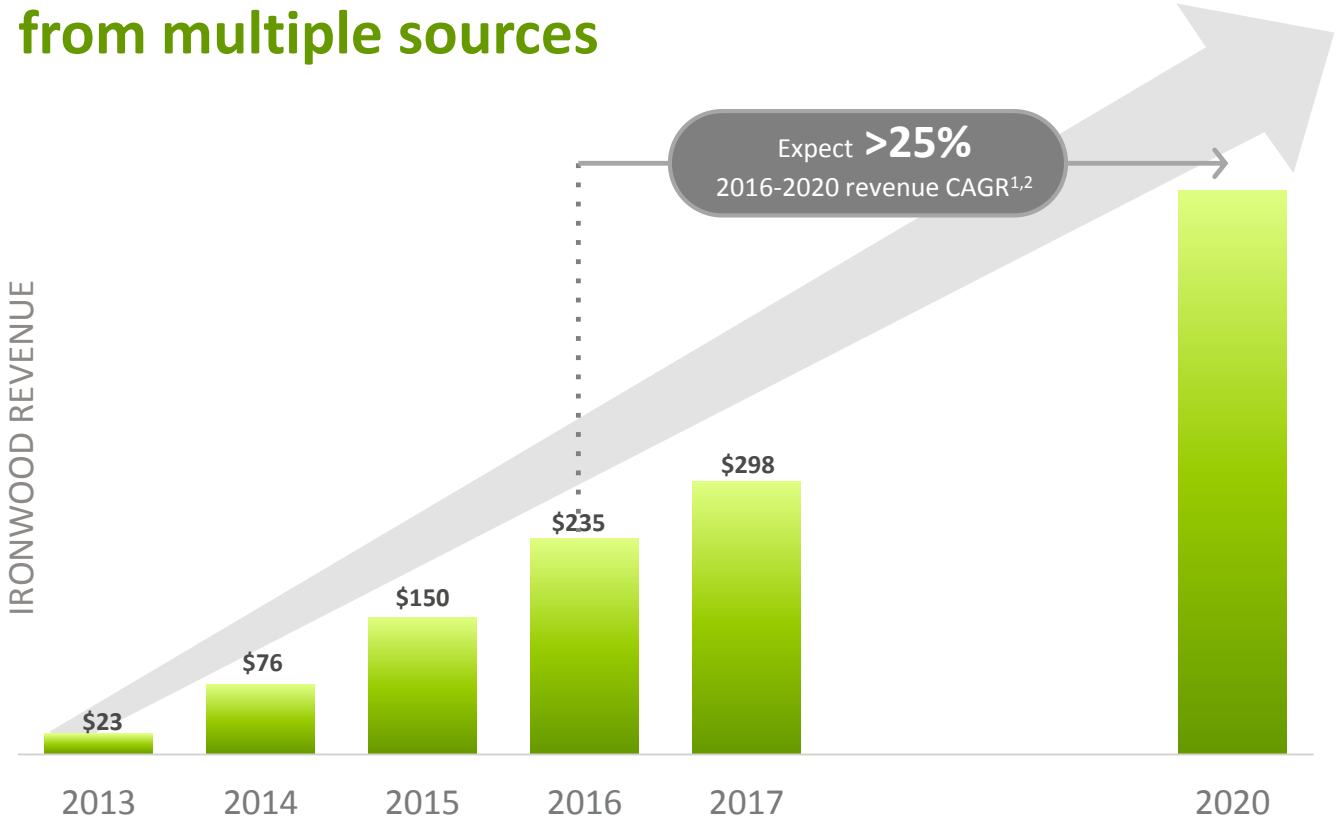
1) The >25% Ironwood revenue CAGR calculation excludes any current or future revenue recognized in the period related to milestone payments to Ironwood, including approximately $39 million recognized in 2016 2) Independent of any new potential partnerships 3) Expect quarterly fluctuations in cash flow

Generating rapid top-line growth from multiple sources



Linzess
U.S. net sales/brand profitability

+

Linzess
Ex-U.S. contribution

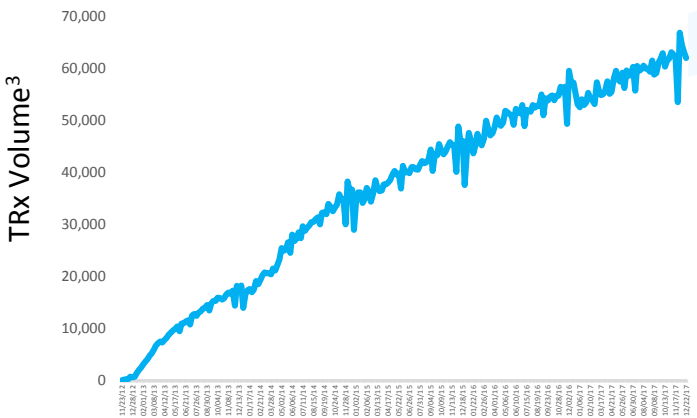
+

DUZALLO
U.S. net sales

1) The >25% Ironwood revenue CAGR calculation excludes any current or future revenue recognized in the period related to milestone payments to Ironwood, including approximately $39 million recognized in 2016 2) Independent of any new potential partnerships

Expecting strong LINZESS growth trajectory into early 2030s

On track to >$1B in annual U.S. net sales with >70% commercial margin by 2020



- **Market-leader:** maintain & strengthen position as branded prescription market leader
- **Millions of patients still suffering:** >2M patients treated[1]; ~40M U.S. adult IBS-C/CIC sufferers[2]
- **Long durability:** IP coverage expected into early 2030s
- **Global opportunity:** significant revenue potential through ex-U.S. partnerships

1) IQVIA Total Patient Tracker Dec-2017 2) Lieberman GI Patient Landscape survey, 2010 3) IQVIA Weekly NPA (12/29/17)

Shaping brand profile by harnessing patient insights

LINZESS: multi-symptom IBS-C/CIC relief, including abdominal pain in IBS-C

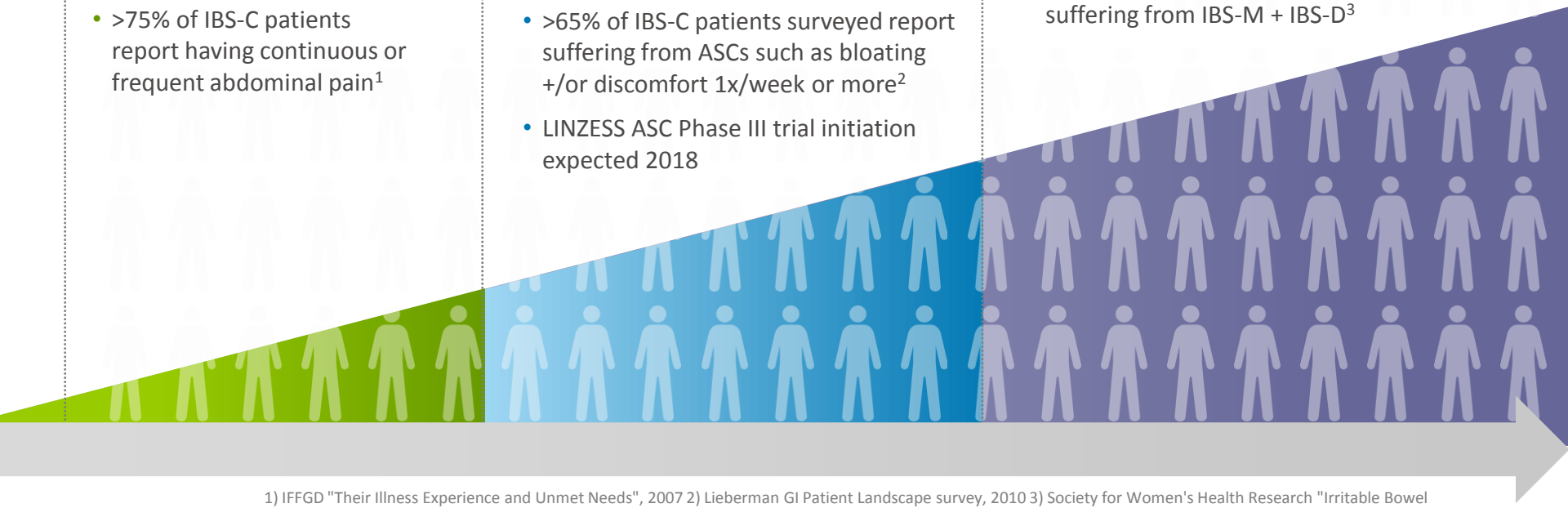
- >75% of IBS-C patients report having continuous or frequent abdominal pain[1]

LINZESS: potential for additional abdominal symptom claims (ASC) to fuel growth

- >65% of IBS-C patients surveyed report suffering from ASCs such as bloating +/or discomfort 1x/week or more[2]
- LINZESS ASC Phase III trial initiation expected 2018

Delayed release: potential to improve abdominal pain relief in all forms of IBS

- Additional 20-25M patients surveyed report suffering from IBS-M + IBS-D[3]



1) IFFGD "Their Illness Experience and Unmet Needs", 2007 2) Lieberman GI Patient Landscape survey, 2010 3) Society for Women's Health Research "Irritable Bowel Syndrome in Women: The Unmet Needs", 2002; Hungin AP, et al. Irritable bowel syndrome in the United States: prevalence, symptom patterns and impact. Aliment Pharmacol Ther. 2005;21:1365-1375; Mearin F, et al "Irritable bowel subtypes according to bowel habit: revisiting the alternating subtype". Eur J Gastroenterol Hepatol 2003: 15: 165-172; Drossman, DA et al "A prospective assessment of bowel habit in irritable bowel syndrome: defining an alternator". Gastroenterology 2005; 128: 580-589

Bringing linaclotide to patients worldwide and capturing significant value from ex-U.S. partnerships

>$260M total revenue from ex-U.S. partnerships (as of 12/31/17)

Astellas-Japan

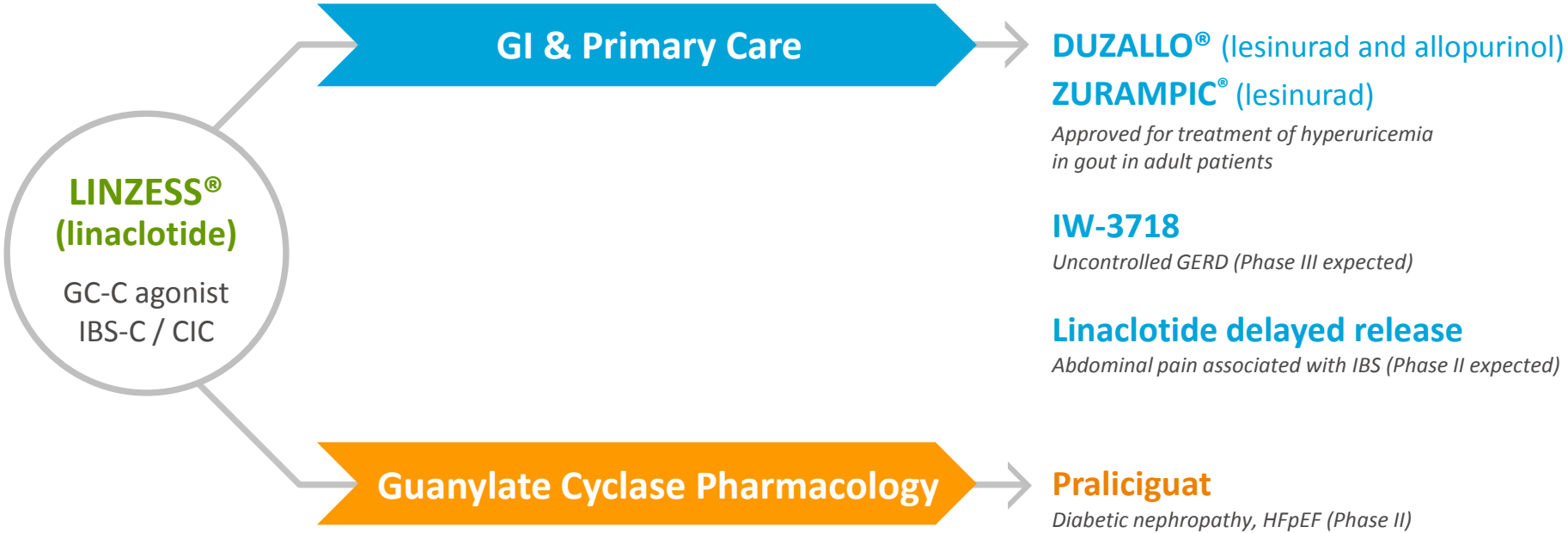
- Strong IBS-C launch; CC approval under review
- Expect >$70M in 2018-2019 revenue from linaclotide API sales to Astellas

AstraZeneca-China

- Approval expected 2018

Innovating productively: leveraging core expertise

Building on Ironwood's pioneering work on linaclotide



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DUZALLO: leveraging customer + market insights as payer coverage expands during launch year

Attractive Market

- ~2M uncontrolled patients[1]
- Highly symptomatic, identifiable patients
- Limited treatment options
- >$300M annual U.S. peak sales opportunity

Learnings

ZURAMPIC

- Lack of payer coverage suppressing uptake
- Monotherapy concern delaying HCP Rx
- HCP lacking urgency to act

Solution

DUZALLO™

- Nearly 2X patients reaching treatment goal[2,3]
- 2 mechanisms to treat disease
- Addresses monotherapy concern
- Simple: 2 products in 1 pill, once a day
- 1 copay for patients

Maximize impact of marketing mix

High performing test markets

High volume adopting physicians
Favorable payer market access

Test (vs paired controls)

- Increased call frequency
- Peer to peer speaker programs
- Targeted consumer advertising

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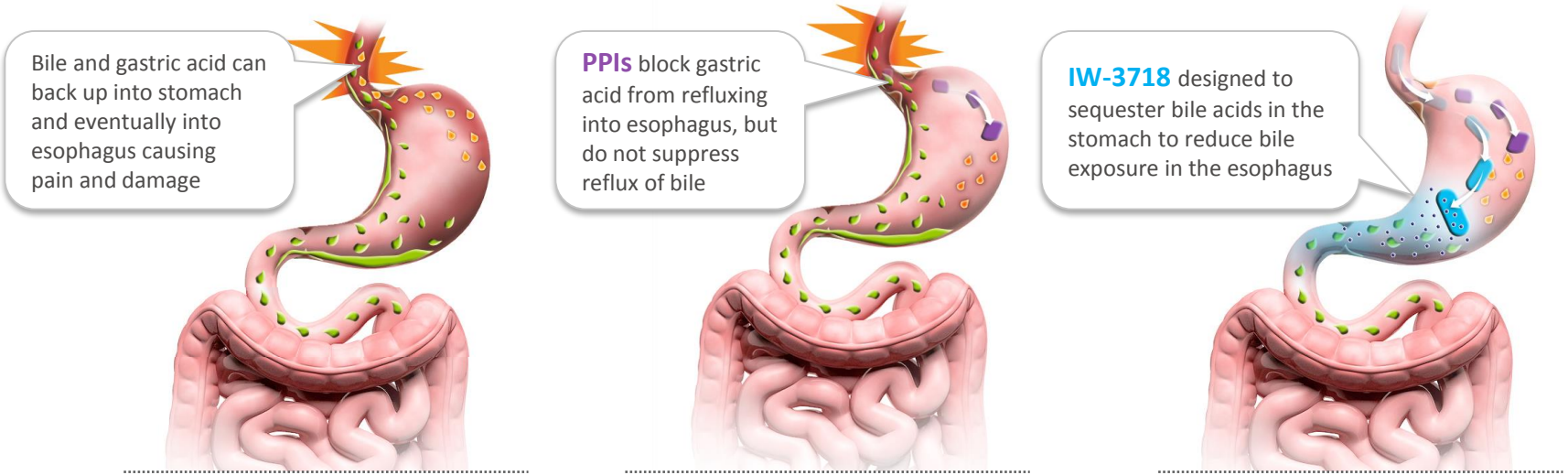
1) 2010 NHANES study estimate, grown at 3% AGR; Juraschek SP et al, Arthritis Care, 2015; Zhu Y et al, Arthritis Rheumatol, 2012; Wood R et al, J Rheumatol, 2016; Khanna P et al, Postgrad Med, 2016; Meyer M et al, Am. J Pharmacy Ben 2015; Primatesta P et al, BMC Musculoskeletal Dis. 2010; Singh JA et al, Arthritis Res & Ther, 2015; AZN/Decision Resource Market Research 2) Allopurinol PI 3) Zurampic PI

IW-3718 presents opportunity to establish new treatment paradigm for uncontrolled GERD

Offers complementary mechanism with PPI, designed to sequester bile acids in stomach over extended period of time



Positive Phase IIb results propelling IW-3718 1500mg towards Phase III

~53%

Patients treated with IW-3718 (+ PPI) reported **clinically meaningful reduction in heartburn severity**

IW-3718 + PPI effect **more pronounced in patients with erosive esophagitis** vs PPI alone

IW-3718 + PPI demonstrated **significant reduction in regurgitation frequency**

Encouraging safety + tolerability; most common AE overall was constipation

Actively working to **accelerate program into Phase III;** trial expected to begin 2H 2018

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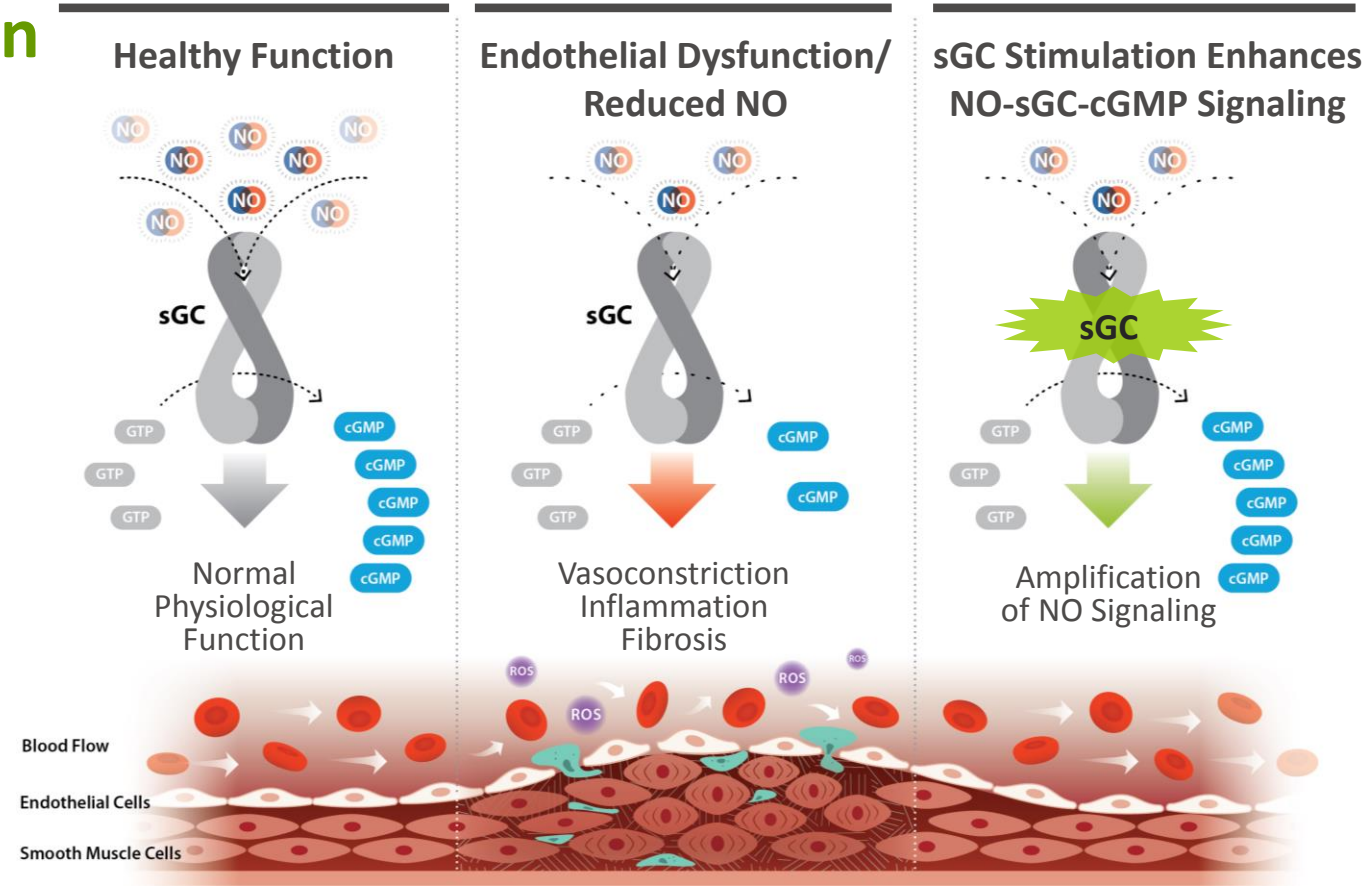
sGC stimulation enhances NO-sGC-cGMP signaling



Praliciguat in Phase II for heart failure with preserved ejection fraction (HFpEF) and for diabetic nephropathy

HFpEF: up to **27M** patients worldwide[1]

Diabetic nephropathy: up to **170M** patients worldwide[2]

- ✓ Highly prevalent form of heart failure; **~40-70% of all heart failure patients** worldwide[3]
- ✓ **Highly symptomatic**; associated with high rates of morbidity and mortality
- ✓ **Prevalence increasing** due to aging population, increasing cardiac/non-cardiac comorbidities[3]
- ✓ **No approved therapies**

- ✓ Diabetic nephropathy is found in **up to 40% of all diabetic patients** worldwide[2]
- ✓ Leading cause of **end-stage renal disease, dialysis and kidney transplants**[4,5]
- ✓ **Risk of progression to renal failure high** despite available treatment options

1) Ziaeian, et al., Epidemiology and Aetiology of Heart Failure, Nature Reviews Cardiology 2016; 2) Gheith et al., Diabetic Kidney Disease: world wide difference of prevalence and risk factors, Journal of Nephropharmacology 2016; 3) Oktay, et al., The Emerging Epidemic of Heart Failure with Preserved Ejection Fraction, Curr Heart Fail Rep 2013; 4) Ghaderian SB, et al., Diabetes and End-Stage Renal Disease; A Review Article on New Concepts, J Renal Inj Prev. 2015; 5) https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease

Phase IIa praliciguat data support desirable drug profile

Multidimensional Pharmacology

Once a day dosing

Encouraging safety + tolerability profile

Broad tissue distribution

Minimal renal clearance

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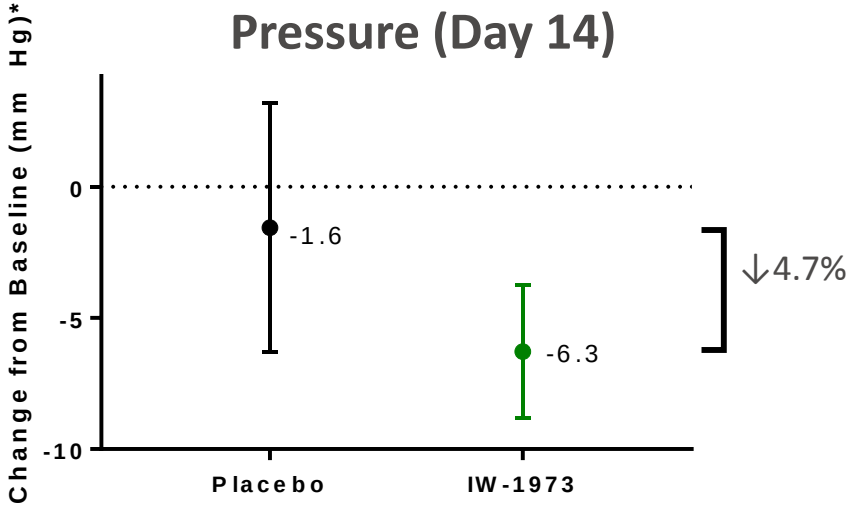
In Phase IIa trial, praliciguat demonstrated positive effects across key biomarkers in cardiovascular and renal disease...

Decrease in Arterial Blood Pressure (Day 14)

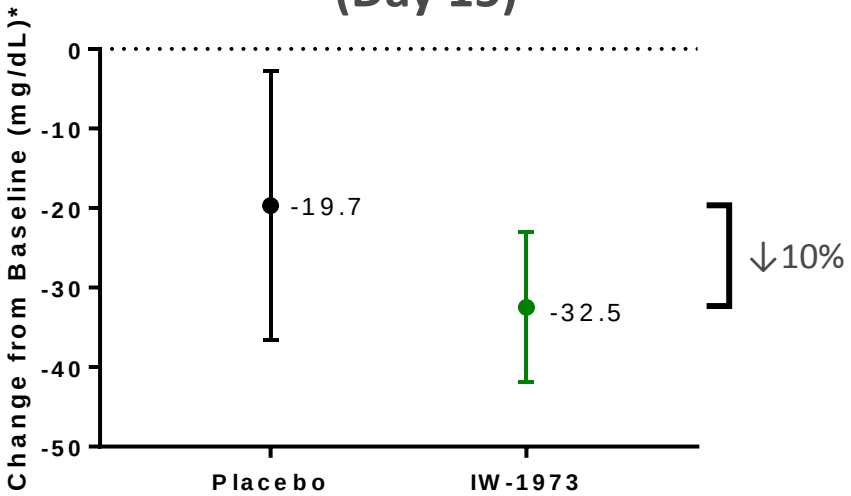


Δ 24h ABPM MAP at day 14

Mean baseline MAP: ~92 mm Hg

**All patients on ACEi or ARB, ~30% on additional antihypertensive Rx*

Decrease in Fasting Glucose (Day 15)



Δ fasting glucose at day 15

Mean (SD) baseline fasting glucose: ~150 mg/dL

**All patients on at least one glucose lowering Rx*

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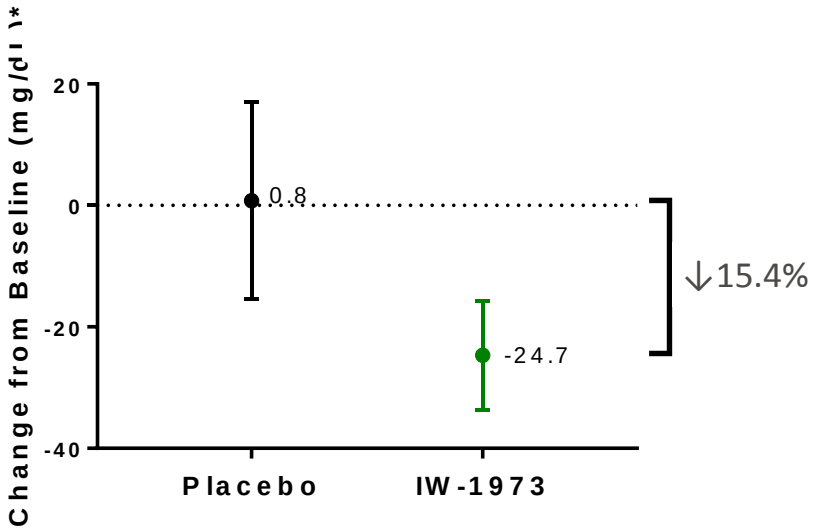
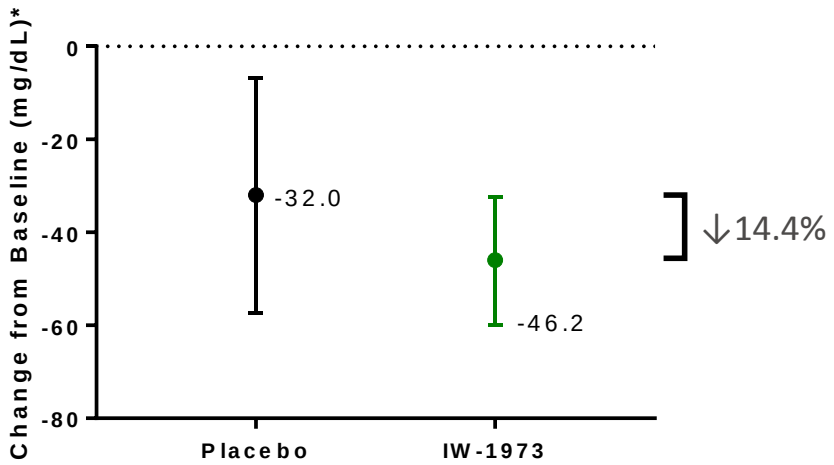
…reinforcing potential treatment effect of praliciguat in diseases such as HFpEF and diabetic nephropathy

Decrease in Cholesterol



Δ serum cholesterol at day 15

Decrease in Triglycerides



Δ serum triglycerides at day 15

Mean (SD) baseline serum triglycerides: ~154 mg/dL

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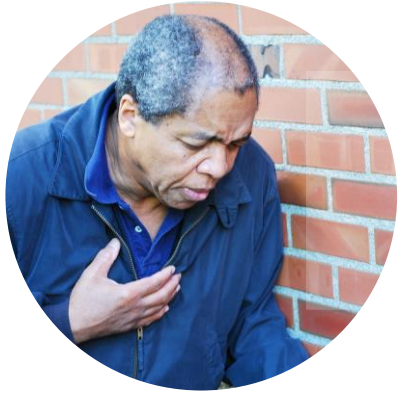
Praliciguat: Increasing blood flow + reducing inflammation, fibrosis and vascular stiffness may improve HFpEF symptoms

CAPACITY-HFpEF Phase II trial ongoing



1:1:1:1 randomization, double-blind

Placebo	praliciguat Low dose	praliciguat Med dose	praliciguat High dose

12-week treatment period

PATIENTS:

- Adult patients with HFpEF (EF ≥ 45%)
- Male and female, age ≥ 50 years
- ~332 HFpEF patients, 4-arms (~83/arm)

ENDPOINTS:

- Change in peak VO2 (CPET) – *primary*
- Safety and tolerability – *primary*
- Change in ventilatory efficiency – *secondary*
- Change in 6-minute walk test (6MWT) – *secondary*
- # of CPET responders – *secondary*

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Praliciguat: Increasing blood flow + reducing inflammation and fibrosis may protect renal function

Diabetic nephropathy Phase II trial ongoing

1:1:1 randomization, double-blind

Placebo	praliciguat Low dose	praliciguat High dose

12-week treatment period

PATIENTS:

- Adult patients with type 2 diabetes mellitus and DN
- Male and female, age 25 – 75 years
- Stable regimen of ACE or ARB
- ~150 patients, 3-arms (~50/arm)

ENDPOINTS:

- Change in urine albumin creatinine ratio (UACR) - *primary*
- Safety and tolerability - *primary*

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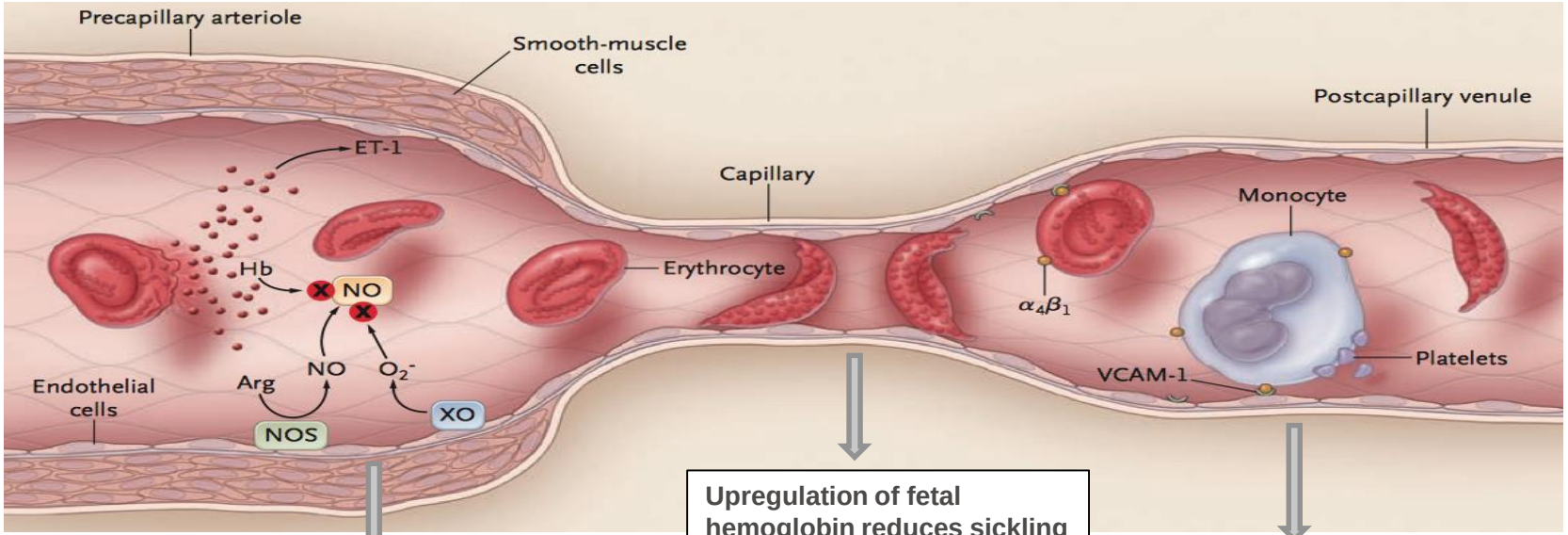
IW-1701 has potential to treat multiple aspects of sickle cell disease pathophysiology



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