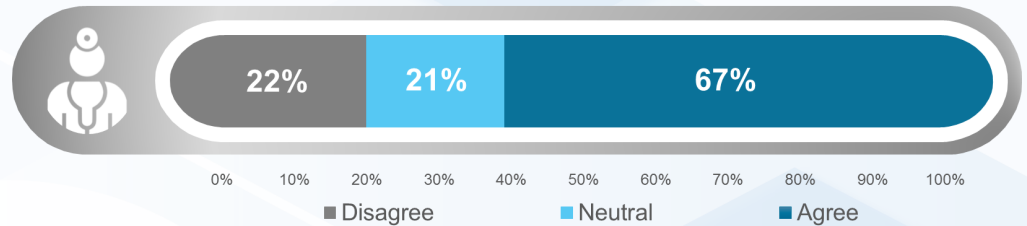


## RealTime Dynamix™: Renal Anemia (US) Q3 2017

The Renal Anemia Market is on the Cusp of Change Beginning with the FDA Approval of Keryx Biopharmaceutical's Auryxia for the Treatment of Iron Deficiency Anemia (IDA) in Adults with Chronic Kidney Disease, Not on Dialysis (CKD-ND). Highlights from this report:

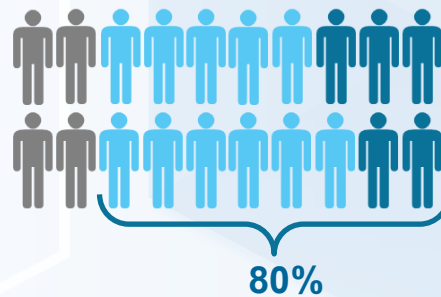
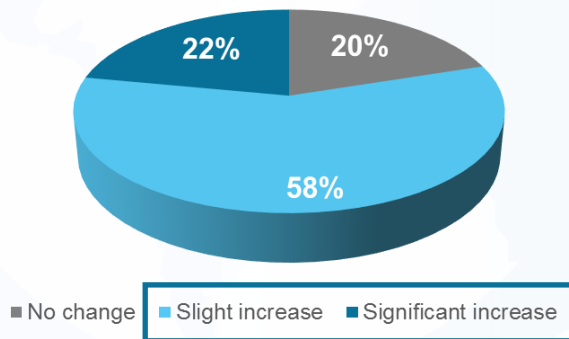
Based on a survey of 194 nephrologists surveyed in September, 67% agree that IV iron is inconvenient for CKD-ND patients.

"IV iron is inconvenient for CKD non-dialysis patients."



80% of the surveyed nephrologists indicated that the approval of Auryxia in IDA for CKD-ND patients would lead to an increase in their use of the brand

### Impact of IDA Indication

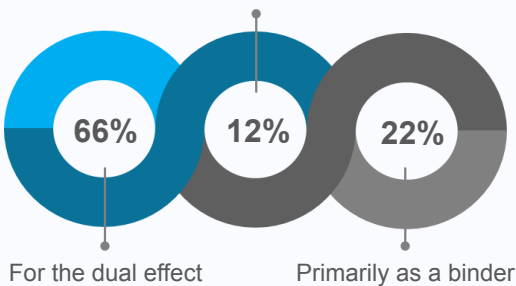


The challenge for Keryx, beyond the ever-present reimbursement hurdles, will be to distinguish Auryxia as an IDA treatment, independent of its phosphate binder indication in dialysis patients.

Among the nephrologists already prescribing Auryxia in the CKD-ND population, the majority prescribe it for the dual effects of phosphate lowering and favorable impact on anemia parameters.

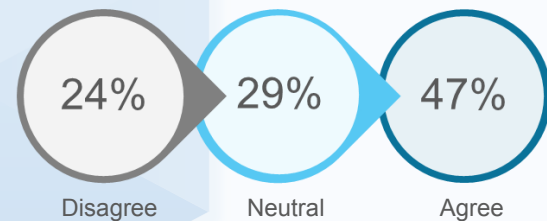
### Use of Auryxia in CKD-ND

Primarily to improve iron parameters



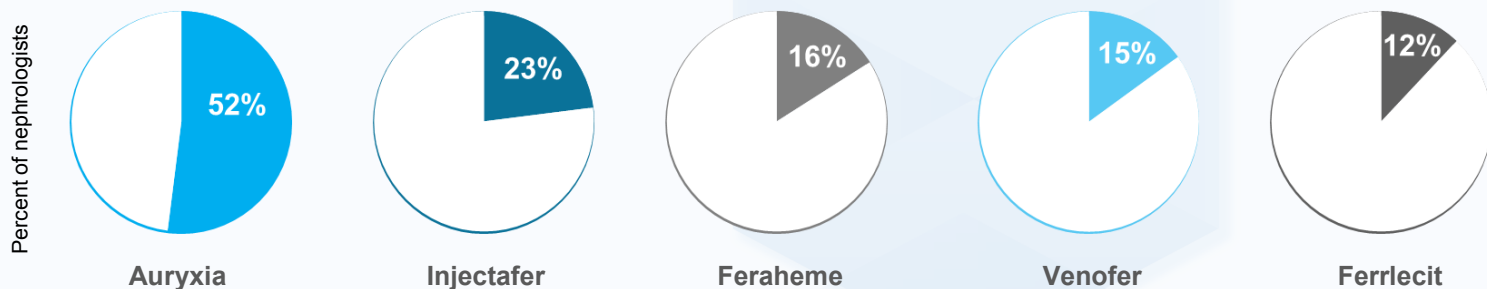
### Distribution of Statement Agreement

"If Auryxia is approved for the treatment of iron-deficiency anemia in CKD non-dialysis, I would only use it if the patient also needs a phosphate binder."



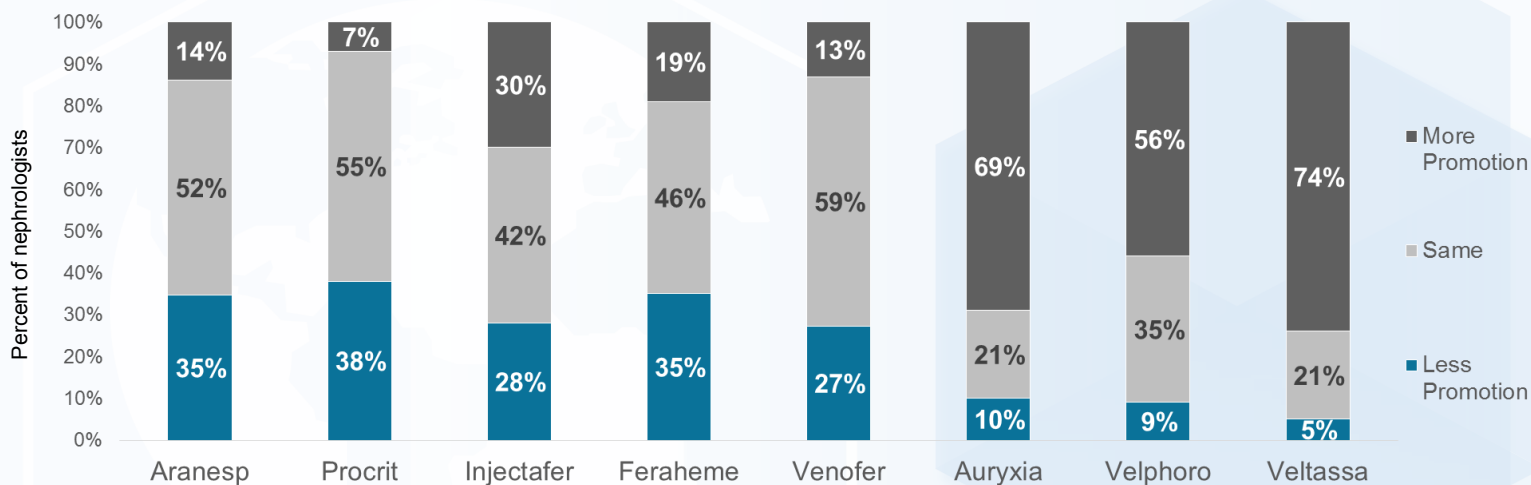
To Keryx's advantage is the current level of promotion overall for Auryxia, which reportedly has increased recently and which vastly outpaces that of IV iron brands such as Daiichi-Sankyo/American Regent/Vifor's Injectafer and AMAG Pharmaceutical's Feraheme.

### Iron Promotion Activity in Past Three Months



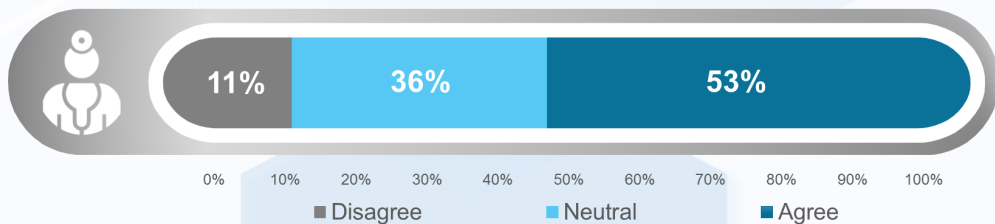
There is little to no promotion of oral iron brands, most of which are generic, leaving Keryx an open runway.

### Shift in Promotion Rates in Past Year



Advancing through the pipeline is a new and novel class of oral anemia treatments known as hypoxia inducible factor -1 (HIF) inhibitors. While nephrologists in the trenches are slowly gaining familiarity with this new class, the excitement about a new approach to treating anemia, beyond the traditional ESA and iron combination, is mounting.

"The availability of HIF inhibitors will revolutionize the way anemia is treated in pre-dialysis patients."



How will these new agents fit in the renal anemia treatment algorithm? According to Jay Wish M.D., Professor of Clinical Medicine at Indiana University School of Medicine...



"Although the HIF stabilizers hold promise for anemia treatment in patients with CKD and especially those not on hemodialysis, such patients still may require some form of iron supplement once endogenous iron stores are mobilized. Since a significant fraction of CKD-ND patients are actually iron depleted, there may be scant iron stores for a HIF stabilizer to mobilize. Even if HIF stabilizers improve absorption of oral iron, it may not be sufficient to meet the needs of increased erythropoiesis, so the combination of HIF stabilizers and a more bioavailable oral iron supplement may be desirable."

## What Else is Happening in Renal?

Nephrologists report changes in practice/policy/reimbursement issues, shifts in dialysis modality to include more home therapies, the KDIGO update to the CKD-MBD guidelines, introduction of Rayaldee, more Acthar/Rituxan/Injectafer/Allopurinol, SPRINT results, finerenone trial and vascular access advances in addition to the more common changes noted below.

### Most Exciting Thing in Nephrology – Past Six Months: Nephrologists' Responses

"Data has come out that the SGLT-2 inhibitors may be beneficial for diabetic nephropathy."

"I am looking forward to using Parsabiv as I think this will make controlling bone disease much easier."

"Evidence that SGLT inhibitors stabilize renal function and have CV benefits. Ability to assign patients with renal anemia to HIF PHI studies."

"Veltassa for hyperkalemia"  
25%

"Bundle changes affecting dialysis companies. Aspects of population nephrology-predicting future of renal practice."

"I think there is an interesting ability to now add on RAAS blockade in patient population that certainly could benefit from it with the use of Veltassa."

"Parsabiv" 10%



"SGLT2's for DN" 5%

"Iron based phosphate binders"  
9%

"IV calcimimetic was approved by the FDA. I would like to prescribe. However, it's not on the dialysis unit formulary. The dialysis unit does not know how to bill for it."

"HIF studies (patients enrolled)" 5%

"Elimination of 6 hr "black box" for Veltassa, making 3 hr window for binding drugs - makes hyperkalemia easier to treat. Also, availability locally of injectafer, making iron repletion easier in CKD."

"I can only think of one specific change and that is dealing with the changes in insurance coverage for my patients."

"Emphasis on more peritoneal dialysis iron based binders with less need for iv iron."

The Q4 wave of *RealTime Dynamix: Renal Anemia* will be published in December. Spherix also covers the bone and mineral metabolism markets (hyperphosphatemia, SHPT), hyperkalemia markets and diabetic kidney disease, in addition to broad based patient audits of over 1,000 dialysis and chronic kidney disease patients for a more holistic understanding of the treatment patterns and opportunities within these segments.



## Renal Anemia (US)

### OVERVIEW

The management of renal anemia in dialysis patients as well as in those with later stage chronic kidney disease is becoming increasingly complex. In the dialysis setting, clinical management is further complicated by a reimbursement model that treats commonly used therapies like erythropoiesis stimulating agents (ESAs) and iron therapies as cost centers. Novel products in development such as the oral HIF-Ph inhibitors offer a new mechanism approach and may change the treatment paradigm in both the dialysis and CKD-ND settings.

This quarterly report series focuses on tracking key performance metrics for ESAs and iron products (oral iron, IV iron and dialysate iron) in both the dialysis and CKD-ND settings. Emphasis is placed on the growing familiarity with pipeline agents as well as the potential role of Keryx's Auryxia as a treatment for iron-deficiency anemia in non-dialysis patients. The rapid field-to insight turnaround, highly relevant content and unparalleled market understanding make **RealTime Dynamix™** an essential tool for companies with commercial products in the space, those that will soon be launching and those looking for business development opportunities in nephrology.

### SAMPLE & METHODOLOGY

Each quarter, ~200 US nephrologists complete an online survey. The respondents are recruited from the Spherix Network, proprietary panel of over 900 US nephrologists. Recruiting is managed to capture a regionally and demographically representative sample.

### KEY QUESTIONS ANSWERED

- What shifts are occurring in renal anemia in the dialysis setting and do these changes vary by chains (i.e. DaVita, FMC)?
- How do treatment rates and approaches for ESAs and IV iron differ between dialysis and CKD-ND patients?
- Do nephrologists have a preference for long-acting or short-acting ESAs and what does this mean for biosimilar ESAs coming to market? Will it impact HIF-PH inhibitor adoption?
- What is the market uptake for Rockwell Medical's Triferic?
- Are nephrologists using Auryxia for the dual action of phosphate lowering and improvement in anemia parameters?
- How does in-office infusion for IV iron or stocking of ESAs influence treatment rates and brand preference?
- How does the unmet need for new anemia drugs compare to the unmet need in other areas of nephrology?
- How are nephrologists becoming familiar with the HIF-PH inhibitors, where will these agents likely play and how will they be differentiated from ESAs and from each other?

### Products Profiled

Auryxia (Keryx), Mircera (Roche, FMC), Venofer (FMC, generics), Injactafer (Vifor, American Regent, Luitpold), Feraheme (AMAG), Ferrlecit, (Sanofi-Genzyme, generics) Aranesp (Amgen), Epogen (Amgen), Procrit (JNJ), Triferic (Rockwell Medical)

**Pipeline:** Retacrit (Hospira, VFMCRP), Daprodustat (GSK), Molidustat (Bayer), Roxadustat (AstraZeneca/Fibrogen/Astellas), Vadadustat (Akebia/Otsuka/Mitsubishi)

### Key Dates

- Q1 March
- Q2 June
- Q3 September
- Q4 December

*Note: a three day embargo is placed on delivery to non-manufacturers allowing clients time to digest the findings before public dissemination*

### Deliverables

- PowerPoint report
- Frequency Table & Summary Statistics
- On-site presentation
- Proprietary questions (for purchasers of the annual series)

### Related Reports 2017

- RealTime Dynamix™ Bone and Mineral US 2017
- RealTime Dynamix™: Renal Anemia EU5
- RealTime Dynamix™: Nurse Practitioners US
- RealWorld Dynamix™: Chronic Kidney Disease US
- RealWorld Dynamix™: Dialysis US
- Market Dynamix™: Renal Anemia

### Pricing

- \$26,500 single quarterly wave
- \$89,500 annual series of four reports