WELCOME NEW AKEBIA (AKBA) SHAREHOLDERS

A CLOSER LOOK AT NEW PHASE 3 DATA SHOWS THAT AKEBIA **MISSED** A CRITICAL TEST, THREATENING NOT ONLY ITS COMMERCIAL PROSPECTS BUT ALSO FDA APPROVAL.

An open letter to new Akebia shareholders…

Dear new Akebia shareholder,

Now that you have participated in the financing, it might be time to conduct some due diligence. You should start by asking Akebia's CEO John Butler a direct and very simple question:

- Was Vadadustat STATISTICALLY INFERIOR to the standard of care with respect to hemoglobin levels in addition to being non-inferior based upon the pre-specified margin?

This is a very simple question with a **"YES" or "NO"** answer—one that was not addressed at all in the company's press release or conference call.

After you get an answer (and let us assure you it won't be the one you are hoping for), you can follow up with this question:

- Is it true that Fibrogen's Roxadustat was STATISTICALLY SUPERIOR to standard of care with respect to hemoglobin levels in addition to being non-inferior based upon the pre-specified margin?

Another very simple question with a **"YES" or "NO"** answer.

Good Luck!

Akebia has a history of omitting key details

- Akebia management seems to ‘forget’ to include key details relating to their operations, clinical data and partnerships.
- These details are only revealed when Akebia management slips them into an SEC filing (typically a 10-K).
  - In the instances we found, Akebia neglected to file an 8-K to disclose theses details in a timely manner, relying instead on the voluminous 10-K filing as **“disclosure camouflage”.**
- Each time the data makes it way out, Akebia shareholders LOSE.
- We believe that Akebia has not disclosed a critical detail regarding their lead program Vadadustat. **IT WAS STATISTICALLY INFERIOR TO STANDARD OF CARE ESA WITH RESPECT TO MAINTAINING HEMOGLOBIN LEVELS.**

We see a clear pattern here with Akebia management: conveniently “forget” to disclose key details in a timely fashion. When detail comes out, stock goes DOWN.

Material Omission #1: Insider Trading

- On June 13, 2016, the Department of Justice filed a criminal complaint against Schultz (Jason) Chan an Akebia employee involved in statistical analysis of clinical trial data.
- The industry press jumped on the matter immediately:


PHARMALOT

Biotech employee charged with insider trading based on study results

By ED SILVERMAN @Pharmalot / JUNE 15, 2016

- Can you guess who **didn't disclose** the existence of the insider trading case, the details of the matter, or the outcome?
  - **AKEBIA MANAGEMENT**

Insider trading calls into question a management team's ability to have adequate controls. Failing to disclose the insider trading to investors is egregious.

Material Omission #2: Mitsubishi Deal

- On December 14, 2015, Akebia management touted a partnership with Mitsubishi on Vadadustat. The deal was described as having a $100MM contribution from Mitsubishi with $40MM paid upon deal signing.
- And AKBA's stock price went up significantly on the announcement:

> **Akebia Therapeutics, Inc.** AKBA gained 7.1% after the company announced that it has entered into a development and commercialization agreement with Mitsubishi Tanabe Pharma Corporation for its lead candidate, vadadustat (formerly AKB-6548), for the treatment of anemia related to chronic kidney disease (CKD) in Japan and certain other countries in Asia.

- When AKBA management *finally* provided the actual details of the Mitsubishi deal in their 2016 10-K, investors were shocked to find that some critical activities ***may not be funded by Mitsubishi***:

Mitsubishi Tanabe Pharma Corporation Collaboration Agreement

Summary of Agreement

On December 11, 2015, the Company and MTPC, entered into a collaboration agreement, the MTPC Agreement, providing MTPC with exclusive development and commercialization rights to vadadustat, the Company's product candidate for the treatment of anemia related to chronic kidney disease, in Japan and certain other Asian countries, collectively, the Territory.

Pursuant to the MTPC Agreement, MTPC has an exclusive license to develop and commercialize vadadustat in the Territory. In addition, the Company will supply vadadustat for both clinical and commercial use in the Territory. The countries included in the Territory are Japan, Taiwan, South Korea, Singapore, Malaysia, India, Indonesia, East Timor, Mongolia, the Philippines, Vietnam, Laos, Cambodia, Thailand, Brunei, Myanmar, Nepal, Sri Lanka, Bangladesh, Bhutan, Maldives, Palau and Tonga and their territories.

In consideration for the exclusive license and other rights contained in the MTPC Agreement, MTPC will make payments totaling up to $350.0 million to fund the vadadustat Phase 3 program (Phase 3 Program), including up to $100.0 million in upfront and development payments, of which $40.0 million was received in January 2016. To the extent Japanese patients are included in the Phase 3 Program, MTPC will fund up to an additional $60.0 million of development costs (Global Scenario). If Japanese patients are not included in the Phase 3 Program (Local Scenario), MTPC will be responsible for the costs of the local Phase 3 study in Japan and make no additional funding payments for the Phase 3 Program. In addition, $20.0 million of the $40.0 million received in 2016 would be used to fund local development of vadadustat in Japan or be refunded to MTPC, at MTPC's discretion.

The final determination of whether Japanese patients can be included in the Phase 3 Program will be made by the Company and MTPC, in consultation with the Pharmaceuticals and Medical Devices Agency, PMDA, following the results of our Phase 2 studies being conducted in Japan, which is expected in the second half of 2017, unless the Company and MTPC otherwise collectively decide, as provided in the MTPC Agreement, to pursue the Local Scenario prior to such determination by the PMDA.

The Company is also eligible to receive up to approximately $250.0 million in additional payments based upon achievement of certain development, regulatory and sales milestones, as well as tiered double-digit royalty payments on sales of vadadustat in the Territory.

Once the 10-K containing these details was released, AKBA shareholders lost ~11% over the next two trading days.

Material Omission #3: Hy's Law

- Akebia filed their 2018 10K on May 23, 2019.
- Buried in the filing was the admission that a patient in the Vadadustat arm of a clinical trial suffered a liver injury classified as a case of Hy's Law. Hy's Law is a highly significant NEGATIVE finding in a clinical trial.

A similar percentage of subjects experienced an AE in the vadadustat and placebo treatment groups (vadadustat 74.6% vs. placebo 73.6%); however, the frequency of certain AEs - diarrhea, nausea, hypertension and hyperkalemia - was greater in the vadadustat arm compared to placebo. In the vadadustat arm, a higher number of subjects reported SAEs of acute and chronic renal failure compared to placebo (9.4% vs. 2.8%, respectively); however, none was considered drug-related by the investigator. The percentage of subjects who had an SAE resulting in dialysis initiation, considered to be a more objective measure of the severity of renal disease, was comparable between vadadustat and placebo groups (8.0% versus 9.7%, respectively) and the number of subjects who discontinued from the study due to AEs of worsening CKD requiring dialysis was also comparable between the vadadustat (4.3%) and placebo (5.6%) groups. One subject with multiple co-morbidities and concomitant medications, including chlorthalidone, had an SAE of liver function test, or LFT, abnormal, considered a case of drug-induced liver injury meeting the biochemical criteria of Hy's Law, which was assessed as probably related to vadadustat. This subject made a complete recovery after vadadustat was discontinued. There were three deaths in vadadustat-treated subjects of which two cardiovascular deaths were considered to be unrelated to vadadustat and one death was attributed to myocardial ischemic and considered by the investigator to be possibly related to vadadustat; no autopsy was performed. There were no deaths in the placebo group.

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- The failure to disclose this in a timely manner is ponderous. The study was completed approximately 4 years before the disclosure. Burying the disclosure in the 2018 10-K without a prior 8-K shows that the Akebia management team has no respect for its investors. The word "Hy's" doesn't even appear in an Akebia filing until 5/23/2019.

- Even the sell side analysts were curious about the omission (from the Q1:2019 conference call):

Alexandre N. Bouilloux, Mizuho Securities USA LLC, Research Division - Research Analyst [7]

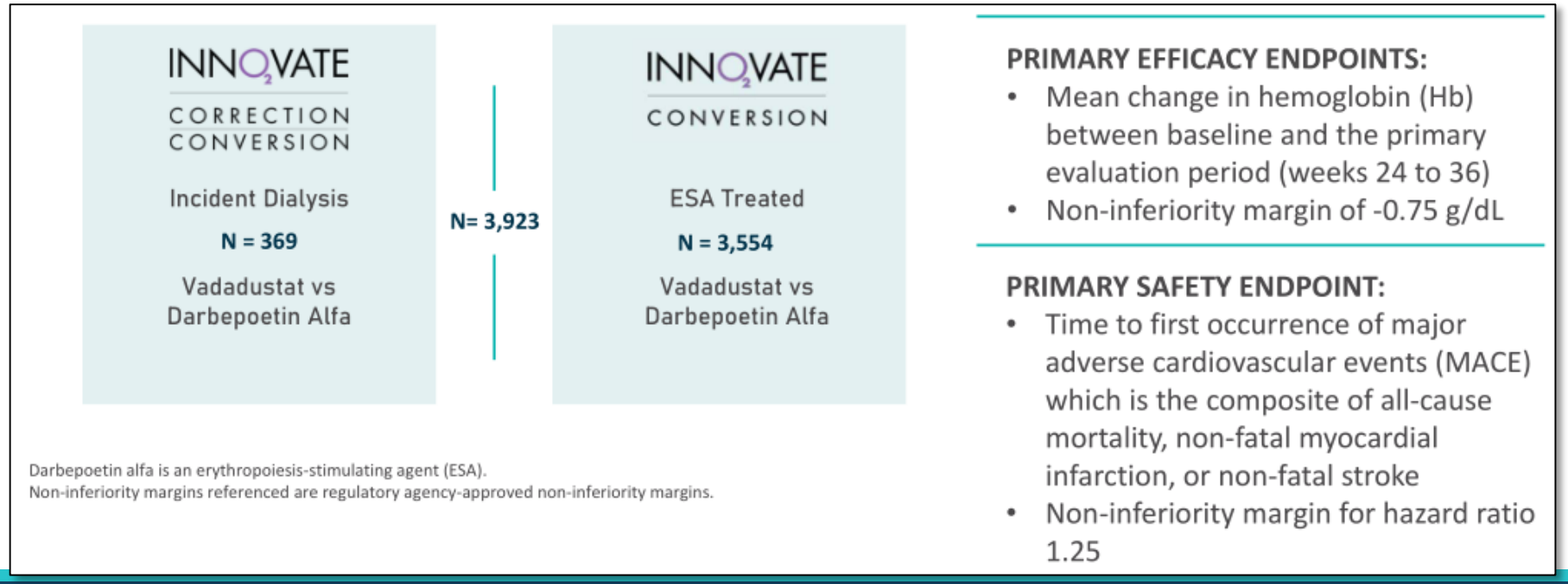
This is Alex on for Difei. I was just wondering if you could comment on the Hy's law disclosure. Maybe if could elaborate a little bit and what gives you confidence you will not encounter a second case?

Akebia shares dropped ~26% over the 10 trading days following the disclosure.

Are you ready for Material Omission #4?

It involves the recently announced INNO$_2$VATE clinical trial results.

- The INNO$_2$VATE study tested nearly 4,000 patients:
  - 3,554 dialysis patients randomized 1:1 to receive either Vadadustat or a standard of care erythropoietin stimulating agent (SOC ESA)
  - 369 incident dialysis patients randomized 1:1 to receive either Vadadustat or a standard of care erythropoietin stimulating agent (SOC ESA)



Summary of data: AKBA vs FGEN

FibroGen

Roxadustat

Akebia THERAPEUTICS

Vadadustat

Performance vs. SOC ESA[1]

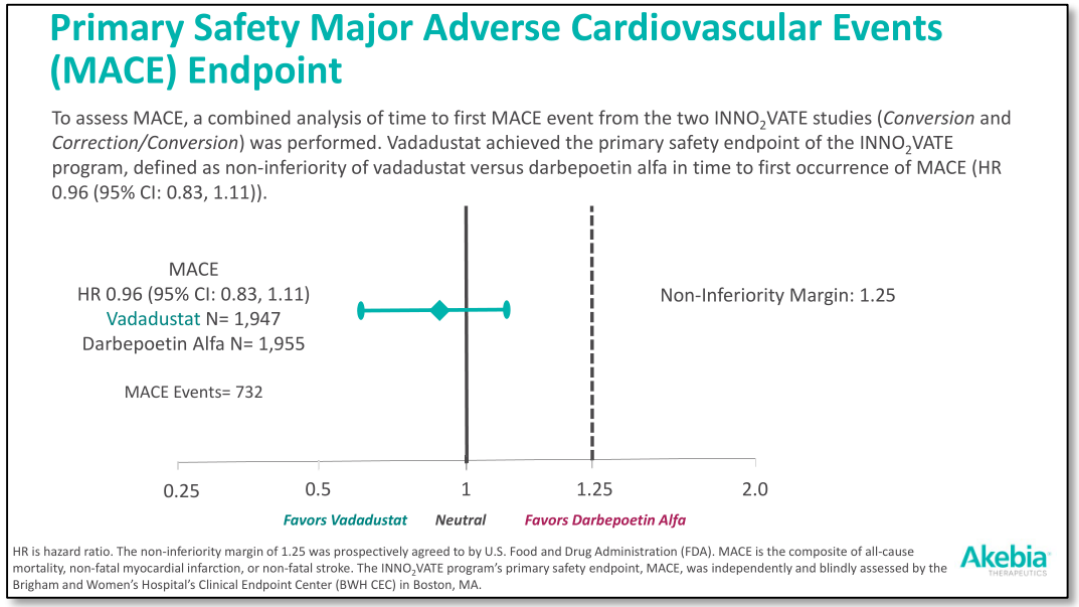
MACE	Hemoglobin (Hb)
Statistically non-inferior HR=0.96	**Statistically significant INCREASE p=0.001**
Statistically non-inferior HR=0.96	**Statistically significant DECREASE p = 0.0000003**

- Both Fibrogen's Roxadustat and Akebia's Vadadustat were shown to be non-inferior to standard of care (ESA) with respect to the MACE outcome endpoint.
- Fibrogen's Roxadustat was also shown to be superior to the SOC ESA with respect to increasing hemoglobin (Hb) levels.
- **HOWEVER, hidden in Akebia's recent Phase 3 data was the fact that Vadadustat was statistically inferior to the ESA control group with respect to maintenance of hemoglobin levels!**

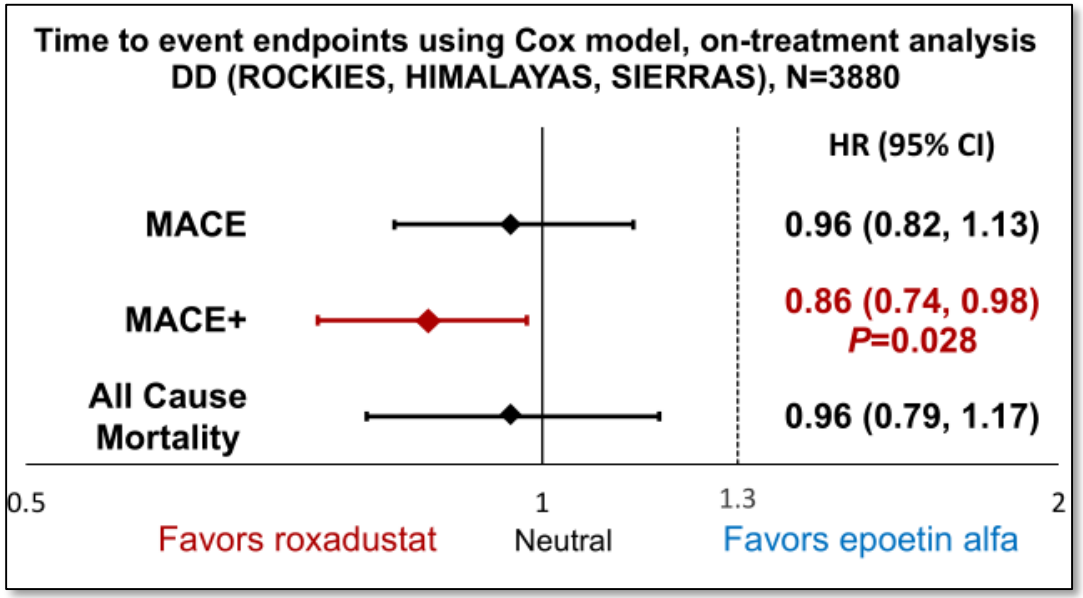
[1] *SOC ESA is Standard of Care Erythropoietin Stimulating Agents such as Aranesp*

Summary of data: MACE Endpoint

- In the data presented on May 5, Akebia management appeared excited to show investors that Vadadustat was clearly non-inferior to SOC ESA with respect to the MACE endpoint. This is similar to data presented by Fibrogen.



Akebia® THERAPEUTICS



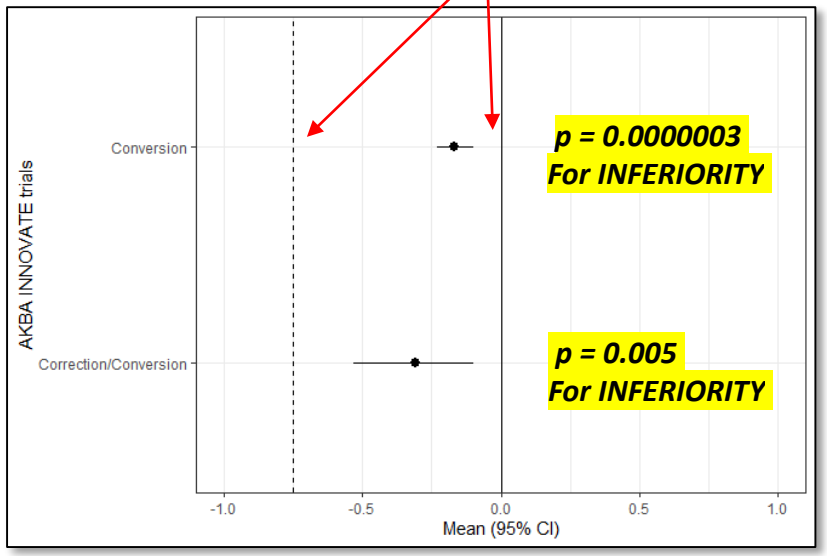
FibroGen

Why wasn't Akebia as excited to show us a similar graph for the hemoglobin (Hb) levels?

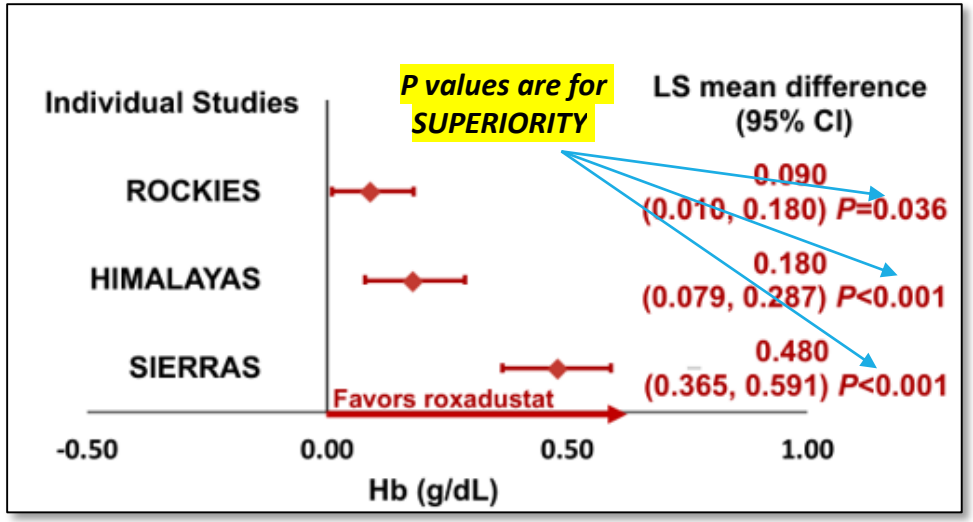
Summary of data: Hemoglobin Endpoint

- Akebia neglected to include a similar slide for Vadudustat vs. ESA with respect to hemoglobin levels, so we created our own **using the data provided in the press release**.
- Fibrogen is the CLEAR winner here as they were able to demonstrate statistical superiority to ESA.

Akebia's data shows vadadustat is simultaneously non-inferior AND STATISTICALLY INFERIOR.



Akebia THERAPEUTICS

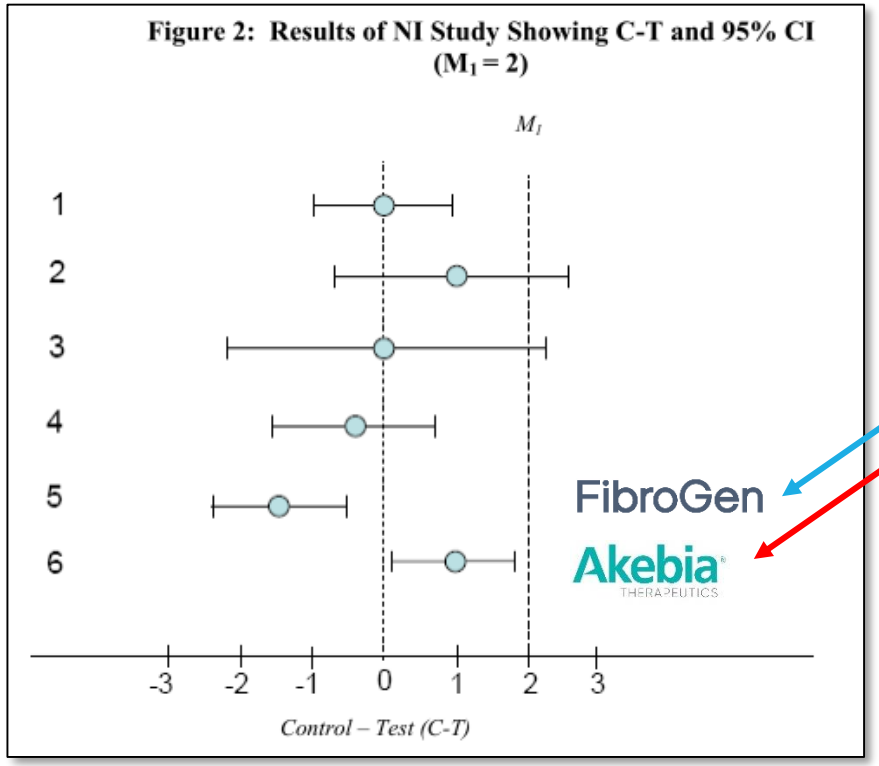


FibroGen

We see that Akebia's Vadudustat is statistically inferior to SOC ESA on hemoglobin production whereas Fibrogen is statistically superior.

Regulatory concerns

- The FDA has already opined on this subject of interpreting inferiority/superiority curves. From the FDA's own guidance documents:



1. Point estimate of C-T is 0, suggesting equal effect; upper bound of the 95% CI for C-T is 1, well below M_1; NI is demonstrated.
2. Point estimate of C-T favors C; upper bound of the 95% CI for C-T is >2, well above M_1; NI is not demonstrated.
3. Point estimate of C-T is zero, suggesting equal effect; but upper bound of the 95% CI for C-T is >2 (i.e., above M_1), so that NI is not demonstrated.
4. Point estimate favors T; NI is demonstrated, but superiority is not demonstrated.
5. Point estimate favors T; superiority and NI are demonstrated.
6. Point estimate of C-T favors C and C is statistically significantly superior to T. Nonetheless, upper bound of the 95% CI for C-T<2 (M_1), so that NI is also demonstrated for the NI margin M_1. (This outcome would be unusual and could present interpretive problems.)

The FDA will have Fibrogen's data in hand when they evaluate Akebia's data. Is there a good reason to approve a statistically inferior product when a superior one exists?

In the FDA's own words, Akebia's outcome versus SOC ESA in hemoglobin production 'could present interpretive problems'.

Summary

- **Akebia is planning to enter a very competitive market dominated by erythropoietin:**
  - Fibrogen has already submitted their NDA for Roxadustat and utilized a Priority Review Voucher.
    - They will have a substantial head start on Akebia
    - They have what appears to be superior data

- Akebia has now provided Fibrogen with the necessary clinical data to successfully market against them.
  - Both agents showed non-inferiority in the MACE endpoint
  - Fibrogen's Roxadustat showed **superiority** in the production of hemoglobin versus SOC ESA whereas Akebia's vadadustat is **inferior**.

- Akebia management will claim Vadadustat satisfied the pre-specified non-inferiority mark for hemoglobin production. **HOWEVER**, as we have shown they are in fact statistically **INFERIOR** to SOC ESA in hemoglobin production.

We think Akebia just handed a huge marketing victory to Fibrogen as Vadadustat is clearly inferior to ESAs on the primary efficacy endpoint. When/if HIFs are approved, we anticipate Vadadustat will be DOA in the marketplace.