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From: Limp, Gerald L

Sent: Monday, January 03, 2005 5:08 PM

To: McKenna, Kevin

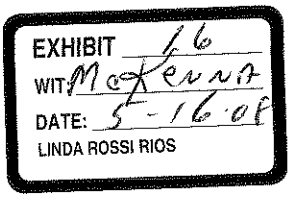
Subject: RE: URGENT PLEASE READ - SEROQUEL - John Patterson Presentation

K, you note on a few slides that we have 'reposed' questions for outstanding issues at the face to face meeting with the FDA on 14 Jan. I wish to leave Dr Patterson with the impression that we will make an attempt to raise these topics, but the FDA has not agreed that these can be addressed during the meeting. I don't want the team that travels to the FDA to be viewed as having failed if we are not successful in gaining FDA's comments on topics other than bipolar depression. This bullet occurs on your slide 2 (FDA interactions - SR) and the bipolar maintenance regulatory risks slide, plus the phase 4 commitments slide. Is reposed a word? If we are unsuccessful in gaining the FDA's input on 14 Jan, then we will begin a regular schedule of contacting the FDA regarding the issues, including filing formal meeting requests as appropriate.

Slide 3/SR - regulatory risks, please note that trial 148 is not currently planned to be conducted.

So far, we've had some difficulty in manufacturing the SR tablets, apparently due to grades/sources of the HPMC that provides the delayed release. This was the cause of early stability failures. We think we've solved that issue, but it is fair to keep in mind that sustained release tablets are in general more difficult to manufacture that immediate release, and we might have a challenging time to get this past the chemistry reviewer. I think the team is confident we can provide an adequate CMC component for the NDA, but I just wish us to keep in mind that this submission is not solely based upon clinical data.

Pat D is out today; the bipolar bits look ok.



You or Meg had started a safety issues slide(s) - do you wish to fold that into this set? For risk mitigation for the glucose utilization issue, please note that we have designed trial 125 to address the topic, although it is enrolling slowly. There are three comparative trials that could add fire to the class, especially due to the fact that 2 are NIH/NIMH trials (the 2 CATIE studies), which adds the perception of impartiality. The other is our trial 114, the CAFE study, which will probably get a fair amount of attention as well. The FDA might be influenced by the findings of these trials, which could result in another round of labeling implications for the participating drug sponsors. There are internal PR plans to address contingencies.

g

-----Original Message-----

From: McKenna, Kevin

Sent: Friday, December 31, 2004 3:15 PM

To: Limp, Gerald L; Boorstein, John (Jack); Bertelsen, Darci L; Groves, Angela J; DeFeo, Pat A; Street, Paul R

Cc: Farina, Daniel

Subject: URGENT PLEASE READ - SEROQUEL - John Patterson Presentation

Importance: High

Dear All,

As some of you are aware, the SEROQUEL GPT is scheduled to present the SEROQUEL LCM program to John Patterson on January 6th from 8-11 am. Based upon a note Meg sent out earlier this week, I have been working to put together slides

on the FDA interactions and regulatory risks/mitigations in the US. I have attached my slides to date. There are still some information outstanding specifically around the pediatric program. I will touch base with Darci on Monday and will have the slides done shortly thereafter.

Paul and Angela are on the distribution list of Meg's note where she assigned potential action items. I ask that you put together the information as best you can with the short notice and competing pressures of the FDA BD rehearsals. I ask that you have your slides together by EOB US time on the 4th. There is a rehearsal in the US from 2-5 pm on the 5th. I'm looking to put together a "risk to the label" slide so if everyone can think of any potential issue from a post-marketing perspective (e.g., diabetes, suicidality, etc) please send them to me. Angela I was thinking of using the Regulatory Defense Work as the basis for the "risk to the label" slides. Please see Meg's draft slide deck as to what I'm referring.

Paul, for guidance on the presentation material, I attached the text of a e-message that I sent to Eva, Bob Holland and Jonas relating to my thoughts on how the team should shape the presentation. I got a positive response from Bob. As you will read in the DC Working Principles Document, an overall assessment of the relationship with regulatory authorities is required. I took a stab of putting slides together for the FDA. You will probably want to do the same for RoW.

Paul and I will need to come up with an overall regulatory risk assessment for each of the LCM programs and one for the overall state of SEROQUEL.

I ask that you please look at the attached slides for accuracy, especially the US folks.

Special thanks to Dan and Jack for pulling the requested FDA background information on short notice.

If anyone has any comments or questions please do not hesitate to contact me.

Kevin

<< File: JSP Presentation_RegSlides12_31.ppt >>

Text of Note to Bob H, Eva and Jonas

Dear All,

I have been giving some thought to the nature, scope, and content of the SEROQUEL Team presentation to John Patterson on January 6th. I'd like to share the tact I believe we should take on the 6th and I welcome your comments on its' validity.

Attached please find a draft Development Committee Working Principles Document dated November 22. Although John and Martin have switched positions since the issuance of the draft, I am comfortable assuming that the DC under John will follow the working principles as defined in the attached. Given that, I would propose that the team tailor the presentation materials around the expectations as put forth for TG3 and TG4 interactions since they seem to best apply to the SEROQUEL LCM program.

At the SMC in Boston during this October, one of the main 4 themes was "Top-line Growth" in the marketed products portfolio. John Patterson is quoted in the November AZ Source as stating that the business is looking to SEROQUEL to deliver $4 billion by 2011. Again for your comment, but I would propose that the team, using the DC Working Principles Document, shape the presentation to address how this will be accomplished through the LCM strategy/tactics currently in place. We could go through the LCM program and for each of the main drug development disciplines (e.g., clinical, commercial, manufacturing (for SR) and regulatory) address strengths/risks and mitigation measures. Other portions of the presentation would be Phase IV commitments/regulatory obligations, "Risks to the Label" (e.g., diabetes, suicidality, etc) and External Environment (risk adverse/heightened Pharmacovigilance HAs, pricing pressures, etc) and, as Meg suggested in her note, there may be some benefit in using the time the team has with John to present the primary care business case.

I'm assuming that John will also bring a PS&L perspective to the meeting on the 6th. I am also guessing that any issues/concerns that Geoff Birkett has raised relative to the LCM program he will have shared with John in his previous role. The team should be prepared for John to raise any issues that Geoff may have.

In a report released right before the holidays, the US Department of Human Health and Services issued a report on importation. It was not favorable for importation with one conclusion being that importation would save US citizens less than 1%. The feeling in the US is that the discussions will now shift towards reference pricing as a means to control costs. If the Medicare/Medicaid Modernization Act were to pass Congress, the reference pricing pressure may abate. Given how SEROQUEL is reimbursed in the US, I believe the team should be prepared to address this issue on the 6th.

The above represents my recommendations for the team to consider and I welcome any thoughts or comments you may have on them. Please feel free to contact me with any questions or comments.

Regards,

Kevin

<< File: DC working group proposal.doc >>