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From: Melville, Margaret G

Sent: Monday, November 01, 2004 11:24 PM

To: Birkett, Geoff; Hoegstedt, Johan; Schwartz, Jack A; Beamish, Don G;

Tugend, Georgia L; Dunscombe, Nick M; Burigatto, Carla; Rastad, Jonas;

Jones, Martin AM (Seroquel)

Cc: Jackson, Marianne

Subject: RE: Field visit observations and follow ups

Dear All,

The team talked last Thursday about Hendersen -- will have a plan in place. Don and Jack will agree the best way to get further information from Dr. Henderson. Jack will discuss how AZ would respond in his upcoming SIMT, and then bring this discussion to the GPT meeting on 23 November. This GPT meeting will focus on the risk log (metabolic and potentially others), which should include a worst-case safety scenario a la Vioxx. After that meeting we'll have a draft plan on how we would respond and timings.

Perhaps Nick could also bring any ideas from Carla, etc. forward as Jack will do from SIMT for GPT in November.

Best Regards,

Margaret (Meg) Melville



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

From: Birkett, Geoff

Sent: Monday, November 01, 2004 6:04 PM

To: Hoegstedt, Johan; Schwartz, Jack A; Beamish, Don G; Tugend, Georgia L;
Dunscombe, Nick M; Burigatto, Carla; Rastad, Jonas; Melville, Margaret G

Cc: Jackson, Marianne

Subject: Re: Field visit observations and follow ups

Team

I agree we need a clear risk mgnt plan and metablism or stroke are areas we need to look at.

On Abilify - can Carla and the PR folks advise what we should do to position Abilify.

Jack Welsh said don't worry about competitors - worry aboiut being competitive , he was often right!

We need to stick to our sales message but de-position them right now - that's what mkt leaders do.

I have some ideas but am keen to hear GPT proposals.

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

From: Hoegstedt, Johan <Johan.Hoegstedt@astrazeneca.com>

To: Schwartz, Jack A <jack.schwartz@astrazeneca.com>; Beamish, Don G <Don.Beamish@astrazeneca.com>; Tugend, Georgia L <georgia.tugend@astrazeneca.com>

CC: Birkett, Geoff <geoff.birkett@astrazeneca.com>; Jackson, Marianne <Marianne.Jackson@astrazeneca.com>

Sent: Sun Oct 31 12:45:15 2004

Subject: Field visit observations and follow ups

This past week I followed your foot steps Jack and was visiting Boston and MGH (mass general). I had some great discussions and out of these came several important take homes that I want to summarize. The first one is especially critical and I want the team, GPT, SLT, or Jack& Don, to set some tight time lines and to develop a clear articulate plan.

Metabolic issue questions. While I was visiting with Dr. Ostacher, who is a Seroquel speaker and strong supporter, he jokingly said something like "well you (Seroquel) will likely be the next one going off the cliff like what happened to Zyprexa this year." I of course followed up and he highlighted some rumors he has heard referring to our metabolic impact and the studies currently being conducted to compare the different profiles - he is not personally involved in any of this work but he did refer to work conducted by Dr. Henderson also at MGH - I don't know if this is the STAR or other trials, but we can't get a false sense of security - if I was at BMS, I would conduct a

metabolic study and possibly include weight gain at max dose Abilify 30 mg vs. Seroquel 800mg, and also include Z and R. I mentioned the comments to Georgia who knows Dr. Henderson well and will follow up with him. This to me this highlights a bigger issue, the criticality of a well prepared risk management plan - we could be under attack tomorrow from one of these small studies and we need to have a response ready and approved within hours - in other words have 98% pre-approved all the way up to David Brennan, David Nicoli, Glenn Gormley, Glenn Engelman, and maybe even Tom. We have talked about this issue, but to me there is no single bigger threat to AZ's growth and prosperity than false and/or misleading information that reach the market place without a strong and appropriate plan by AZ - and I would propose that we give this challenge to a dedicated team (PR, attorney, MD..., and possibly also include external and other cross functional AZ risk mgt expertise) and ask them to have a draft plan within 2 weeks and a full articulated plan based on key possible scenarios by year end (should also include the appropriate response to KATIE(?), a Sidney Wolf attack...). I also believe we should do what is possibly to accelerate our own data, look to recruit faster and broader for STAR, look at adding more diverse populations or conduct a second trial in diverse populations since weight and metabolic issues may be more prevalent in this population. I also would be interested in what we believe is the right maintenance dose for bipolar disorder and how we should start communicating the right dose for long term use since Seroquel's profile looked so much better at 300 mg in Bolder 1. I also do believe that metabolic issues are and will be a long term concern (for all or at least most atypicals) and every KOL I met believe that atypicals are a great addition to refractory or severe depression patients but not a replacement and they are already using them in this setting to a limited extent.

On the unipolar depression point - Jack, I know you met with some of the folks and the chairman at MGH, Rosenbaum (SP?), and others (Fava...) mentioned that they would be delighted to put together a small advisory type of meeting at MGH to discuss our LCM plans and have some of our Seroquel leaders fly up there. They could do this very quickly and it may be a great opportunity to get feedback from some strong Seroquel supporters but also from the top ranked Psychiatry department in the country.

At Tufts I met with their new department head Dr. Summergrad who came from MGH and we could possibly involve him in some of the discussions. He also brought Dr. Hsu to the discussions and apparently Dr. Hsu has one of the largest Asian Psychiatry practices in the country - we may consider adding him for example in the STAR trial or in a possibly second trial. I also met with Ron Hammer who is very involved in Pharmacology and Georgia maybe you can have the MIS follow up directly with Dr. Hammer as he started asking me question way beyond my technical expertise - his contact info is available below.

Lastly, per my note around Abilify - everyone is starting to swing against us and how/where do we want to position Abilify for the future? I got a sense that they may already be conducting some Unipolar depression work - no strong CI though. If we play this right I could see a world two years from now when Seroquel has 30-35% share and Abilify and Risperdal is fighting for the #2 spot at 15-20%, but we need to position them right today and based on their Mania label they are vulnerable right now.

Love to catch up on these issues ASAP - I included you Geoff since I know you have talked to the GPT members around the risk mgt team and you Marianne since we were visiting with many of your and Georgia's customers.

Johan

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

From: Clemens, Richard A

Sent: Friday, October 29, 2004 10:49 AM

To: Hoegstedt, Johan

Subject: FW: Ron Hammer

Email for Dr. Hammer - rhammer@tufts-nemc.org

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