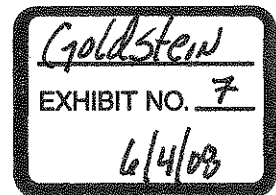


Fax 151 794 2945

Goldstein Jeffrey J

From: Goldstein Jeffrey J
Sent: Monday, November 17, 1997 8:57 AM
To: Czupryna Michael MJ
Subject: FW: Drug discrimination studies with seroquel



Mike,

Here is Goodies reply to my note about not funding his research. He is now requesting a 22 g sample to complete his studies which he is funding himself (?). Can we supply such a quantity?

Jeff

Jeffrey M. Goldstein, Ph.D.
Assistant Director MRCG
Ext. 8071

From: Andrew Goudie (SMTP:ajg@liverpool.ac.uk)
Sent: Friday, November 14, 1997 10:01 AM
To: Goldstein Jeffrey J
Subject: RE: Drug discrimination studies with seroquel

Dear Jeff,

I was VERY sorry indeed that Zeneca are unable to fund any work with Seroquel. However, we are STILL interested in pursuing such work in two separate ways in studies which we will fund ourselves IF and only IF Zeneca are able to supply us with Seroquel:-

i) By the study of the discriminative stimulus properties of Seroquel itself.

This would require us to train up 2 groups of 14 rats each on 5 and 10 mg/kg of Seroquel. To do this and study the stimulus properties of Seroquel over a period of some 18 months (including training) we estimate that we would need some 18 gms of the drug.

ii) By the study of the development of cross-tolerance to the stimulus properties of clozapine. Briefly, we have shown that in rats trained to discriminate clozapine, b.i.d. treatment with high doses of clozapine results in pharmacodynamic tolerance to clozapine. We now wish to study the specificity of this effect, and see if agents such as Seroquel, which generalise to clozapine, also induce cross-tolerance to clozapine. This study would involve b.i.d. treatment with Seroquel at 20 mg/kg for 20 days and would require some 4 gms of

Seroquel.

Would Zeneca consider providing us with as much as 22 gms of Seroquel? We would really like to pursue these studies and feel sure that the results would be of very great value to you in showing YET AGAIN that Seroquel is definitively clozapine-like!

I look forward to hearing from you at you earliest possible convenience.

Sincerely,

Dr Andrew Goudie

>
> Dear Andrew,
>
> There are a number of preclinical research proposals that are awaiting
> funding decisions. I had hoped to bring these to the attention of the
> Seroquel Board for resolution at our last meeting. But due to the number
> of agenda items and the limited time for discussion, this topic was
> tabled for the next meeting.
>
> I think it is fair to say that the decision to fund any further
> preclinical work will depend on the competitive advantage that the work
> can demonstrate for Seroquel (like your drug discrimination results that
> clearly demonstrated Seroquel was closest to clozapine and different
> from the other atypicals). This is primarily due to the fact that R&D is
> no longer responsible for Seroquel research - it is now the
> responsibility of Sales and Marketing. So preclinical research studies
> aimed at mode of action, although very interesting to both of us, do not
> translate to marketable messages that will impact sales (at least this
> is what my commercial colleagues say). On the other hand, clinical
> studies that extend the indications for Seroquel can directly impact
> sales. With limited budgets, funding of clinical studies will therefore
> come first.
>
> I sincerely appreciate the work that you have done thus far on Seroquel,
> and I hope that you can continue to do additional research with
> Seroquel, even if it cannot be directly funded by Zeneca. I am still
> trying to convince my commercial colleagues of the need and value of
> preclinical research for the life cycle management of Seroquel. I will
> let you know if things change. But for now, there is no support
> available for the studies that you have outlined.
>
> Sorry that the news is not better.
>
> Sincerely,
>
> Jeff
>

> Jeffrey M. Goldstein, Ph.D.
> Assistant Director MRCG
> Ext. 8071
>
> -----