January 26, 2009

Christi L. Stark, M.S.
Regulatory Project Manager
U.S. Food & Drug Administration
CDER/OND/ODEIII/HFD-180
White Oak, Bldg. 22, Room 5137
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: IND # 104,116 Cassidy Hempel
Request for a Type A meeting

Dear Ms. Stark:

On 1/21/2009 we sent to Dr. He our complete responses to the clinical hold notification for IND # 104,116 C.H. We are requesting a Type A meeting with the Division to discuss this response and to reach agreement on any outstanding issues that may be necessary to resolve in order to begin treatment under this compassionate use IND.

We would like to propose any one of the following dates for the meeting: February 2, 6, 10, 11, 23, or 27.

We would like to request that someone from the FDA familiar with the safety of cyclodextrin based upon other regulatory filings be in attendance. In addition, if anyone at the FDA is familiar with Niemann-Pick Type C (NPC) disease, their presence would be beneficial. Perhaps someone from the Orphan Drug division would also be appropriate?

We propose the following people will attend the meeting:

- Chris and Hugh Hempel, parents of the NPC children covered by this IND #104,116 C.H. (and IND #104,114 A.H.).
- Several other parents of NPC children have expressed an interest in attending this meeting if feasible.

- Dr. Caroline Hastings, MD, the investigator who will treat the children.
- Dr. Ron Browne, Ph.D., consultant
- Ms. Amy Marcus

Re: IND # 104,116 C.H.
Request for a Type A meeting

Questions to be addressed at the meeting include:

Does the Division agree that patients with NPC disease qualify for compassionate use therapies, given that there are no approved drugs for this condition?

1. Does the Division agree that there exists in the literature and previous regulatory filings sufficient safety data to permit treating NPC patients with hydroxyl-propyl-beta-cyclodextrin (HPBCD) intravenously?
2. Does the Division agree that a reasonable starting dose of HPBCD would be 20mg/kg/hr at a rate of 20ml/hr?
3. Does the Division agree that the methods for preparation of the HPBCD for infusion are appropriate?
4. Does the Division agree that a continuous infusion for four days is appropriate?
5. Does the Division agree that the safety monitoring and stopping procedures specified in the revised treatment plan are sufficient?
6. Does the Division have suggestions for subsequent dosing and dose escalation?
7. Does the Division have suggestions as to maximum daily dose, assuming the absence of grade 3 toxicity during previous doses?
8. Does the Division agree that a 6 month treatment period is acceptable?
9. Does the Division have any suggestions concerning therapeutic endpoints other that those specified in the revised treatment plan?

I look forward to receiving your reply to this request along with the separate request for IND #104,114 A.H. which accompanies this letter.

Sincerely,

Caroline Hastings, M.D.
Director, Fellowship Program
Children's Hospital & Research Center Oakland
747 52nd Street
Oakland, CA 94609-1809

Tel: (510) 428-3631
Fax.(510) 601-3916

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White Oak, Bldg. 22, Room 5137
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: IND # 104,114 Addison Hempel
Request for a Type A meeting

Dear Ms. Stark:

On 1/22/2009 we sent to Dr. He our complete responses to the clinical hold notification for IND # 104,114 A.H.. We are requesting a Type A meeting with the Division to discuss this response and to reach agreement on any outstanding issues that may be necessary to resolve in order to begin treatment under this compassionate use IND.

We would like to propose any one of the following dates for the meeting: February 2, 6, 10, 11, 23, or 27.

We would like to request that someone from the FDA familiar with the safety of cyclodextrin based upon other regulatory filings be in attendance. In addition, if anyone at the FDA is familiar with Niemann-Pick Type C (NPC) disease, their presence would be beneficial. Perhaps someone from the Orphan Drug division would also be appropriate?

We propose the following people will attend the meeting:

- Chris and Hugh Hempel, parents of the NPC children covered by this IND #104,116 C.H. (and IND #104,114 A.H.).
- Several other parents of NPC children have expressed an interest in attending this meeting if feasible.
- Dr. Caroline Hastings, MD, the investigator who will treat the children.
- Dr. Ron Browne, Ph.D., consultant
- Ms. Amy Marcus

Re: IND # 104,114 A.H.
Request for a Type A meeting

Questions to be addressed at the meeting include:

Does the Division agree that patients with NPC disease qualify for compassionate use therapies, given that there are no approved drugs for this condition?

10. Does the Division agree that there exists in the literature and previous regulatory filings sufficient safety data to permit treating NPC patients with hydroxyl-propyl-beta-cyclodextrin (HPBCD) intravenously?
11. Does the Division agree that a reasonable starting dose of HPBCD would be 20mg/kg/hr at a rate of 20ml/hr?
12. Does the Division agree that the methods for preparation of the HPBCD for infusion are appropriate?
13. Does the Division agree that a continuous infusion for four days is appropriate?
14. Does the Division agree that the safety monitoring and stopping procedures specified in the revised treatment plan are sufficient?
15. Does the Division have suggestions for subsequent dosing and dose escalation?
16. Does the Division have suggestions as to maximum daily dose, assuming the absence of grade 3 toxicity during previous doses?
17. Does the Division agree that a 6 month treatment period is acceptable?
18. Does the Division have any suggestions concerning therapeutic endpoints other that those specified in the revised treatment plan?

I look forward to receiving your reply to this request along with the separate request for IND #104,116 C.H. which accompanies this letter.

Sincerely,

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