CTSF
Cure Tay-Sachs Foundation

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Research Update – August 2015

Research summary

Let's talk about the reason we do all this work (or passion in some cases) - to beat this f'n disease!! Excuse my language. We fund the research that shows promise to treat or cure Tay-Sachs disease - that is our Mission Statement. Plain and simple. We are single minded with our eye on the prize. Currently we have two promising research projects underway and I have updates on both of them. Both updates are good news!!

First **UC Davis**. The CTSF is funding 100% of this research project. To date we have funded **$343,866** with another **$112,901** committed to the project. The team got off to a slow start and has re-organized not once but twice - but they seem to be hitting their stride now. The following is the update provided by the team for public release:

I wanted to give you an update on the progress of our TS project. It has been moving along nicely. Here are the main points that we have accomplished since we last talked.

1. *Yesterday, we finished transplanting the last litter of mice for our long-term (6-month) study to evaluate the safety of the vector transduced human HSC. (Aim 3 of our proposal). The transplanted mice will need to go for 6 months before we can evaluate them for the cells' engraftment and multi-lineage hematopoiesis.*
2. *We currently have 15 Sandhoff mice transplanted with therapeutic vector transduced cells and will be transplanting control vector transduced cells this coming week. These 15 mice were transplanted as newborn pups to try and increase engraftment of the transduced cells and to increase efficacy from what we have observed so far.*
3. *Today we obtained more in vitro safety data from vector transduced TS fibroblasts demonstrating that the vector does not have any deletions or rearrangements after transduction of cells.*
4. *In the next 1-1.5 months, we will be completing the rest of the in vitro safety data which includes and in vitro immortalization assay to rule out any oncogenic effects of the vector integrations, a CFU assay to make sure vector transduced cells differentiate properly, and two more expression assays to detect expression of HexA and HexB in the vector transduced cells.*
5. *This past week we completed an experiment to evaluate the effectiveness of our vector transduced cells to cleave synthetic substrates (MUG/MUGS). This experiment mimics the degradation of GM2.*

We are continuing to move forward as quickly as possible. I believe that with good safety data, we will still be able to have a pre-IND meeting with the FDA. As we have mentioned before, they are mostly worried about safety and as long as the gene modified cells are safe, we may be able to move toward a clinical trial. We have shown effectiveness, just not any prolonged lifespan in the mice. The vectors obviously work though both in vitro at cleaving the synthetic substrate and also in the mice by decreasing the GM2 aggregates

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To summarize all that for you. The team is showing that the vectors they are using are removing GM2 from the brain. The challenge is the expression on Hex A is still fairly low - but improving. They have not extended the life of an affected mouse yet - but are impacting the disease. The team is very excited about the progress - we'll get another update in a couple of months.

The **Tay-Sachs Gene Therapy Consortium** (the group we've spent $1.2 million on so far - with another $330,407 committed) is also very excited about recent developments - I spoke with Miguel yesterday. As we had discussed earlier the team was seeking guidance from the FDA after the successful primate tests with the new vectors. We need to know what they would like to see in order to approve our clinical trial. Miguel says the FDA provided the most detailed feedback he'd ever received - in essence they gave us a roadmap to clinical trials. And most of thier requests included testing the team has already done successfully. Basically the FDA wants a series of independent tests (probably to be done at Univ of FL) to verify our findings. They want some studies that could take up to a year, but the FDA makes a point to say the clinical trial can begin before those studies are complete. The team is ready to get moving NOW!! They just need a couple weeks to work out all the details - and create a budget. Miguel is very confident the independent studies will be successful - he's already done most of the tests. And his estimation is we have 6 to 8 months of work ahead of us. To sum all this up - the FDA asked us to do the following before they will approve a clincial trial, we are confident the studies will go well, and the FDA is on board with our plan. The chance a clincial trial could start in 2016 is encouraging. I changed that word a couple of times - I don't want to get everyones hopes up since we have seen so many delays - but I will tell you Miguel is more than a little excited. We sure could use smooth sailing from here. Fingers crossed.

So we have two different research teams both talking about clincial trials. This is not me putting words into their mouths or pressuring them to go faster. I have very much stayed out of the research direction and we've let the experts make the decisions and set the timeline. I am sure we have more unknown hurdles ahead of us - but we have a lot of testing and expertise in our corner now. This is good news - trust me.

This update will be posted on the Cure Tay-Sachs website under Quarterly Updates. You can also learn more about the TSGT at www.tsgtconsortium.com. If you have any questions or comments about this update I can be reached at ken.bihn@curetay-sachs.org or you can call the foundation offices at (216) 812-5855

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