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Research Update – March 2010

The Tay-Sachs Gene Therapy Consortium (TSGT) has issued a research progress reports for public release (see attached) and it could mark the beginning of some meaningful progress with a large animal model. The Cure Tay-Sachs Foundation has spent \$300,000 in support of the TSGT and the NIH awarded them a four year, \$3.5 million grant in August 2009.

As background, to move an experimental therapy from the lab to the bedside researchers must show success in a small animal model and a large animal model. There are also toxicity studies and other hurdles to clear before the FDA will approve a human clinical trial, but a working large animal model is a hurdle Tay-Sachs therapies have not been able to clear. For our therapy the large animal model is to treat a naturally born affected cat – that is why the Cure Tay-Sachs Foundation has dubbed 2010 “**The Year of the Cat**”. Additionally, there is a herd of Jacobs sheep (another potential large animal model) naturally afflicted with Tay-Sachs disease – but preparing sheep for clinical use was thought to be six to twelve months away. We have great news on that front as well. Here are some of the research highlights – for the full public release read the attachment:

(There are two kinds of cats in our research – GM1 and GM2 - both are lysosomal storage diseases. The GM1 cats are more plentiful, but the GM2 cats are the better Sandhoff/Tay-Sachs model. We expect both conditions to be helped by our gene therapy treatment.)

- In September 2009 a GM1 cat was born and treated with our gene therapy. Today, six and a half months later, a veterinary neurologist sees NO signs of GM1 disease!! An untreated GM1 cat normally begins showing signs at three and a half to four months. A number of treated GM1 cats are currently in the pipeline. This is VERY encouraging!!
- A GM2 cat was born and treated in January 2010. At two months of age the cat continues to do very well. It is still too early to say the treatment is a success – but at two to two and a half months an untreated cat normally displays whole body tremors – this cat does not. We’ll know better in four



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- months, but again this progress is very encouraging. Another GM2 cat was treated in late March 2010 – so we now have two treated cats to study.
- As the research team waits on additional GM2 births, they have injected gene therapy vectors into a carrier cat (one good gene and one mutated gene). One month after injection the enzyme levels in the brain and central nervous system were 60-fold higher!! If you took a Tay-Sachs child with a 2% Hex A level and increased it to 4% - it would translate into years more life. If it went up 60 times – that would stop the disease progression all together!! Increased enzyme expression in the central nervous system is also VERY encouraging.
 - The Tay-Sachs sheep colony has produced four affected lambs that are candidates for gene therapy. The research team is creating a sheep vector model and hopes to treat these animals very soon – well ahead of the original plan.

This is very exciting (and very preliminary) research data. We have what appears to be a working large animal model and now an additional large animal model is research ready well ahead of projections. The next three to six months will be critical for our pioneering cats!! It is still possible the treatment impact will fade or the disease is just progressing slowly in our treated cats – we have our fingers crossed!! Today – we have hope!!

Even more good news, the NTSAD is in the final phase of review for research proposals seeking monies. There are a number of very exciting proposals being reviewed by the Scientific Advisory Committee and the Research Initiative team; including a highly scored stem cell project and a sheep research project. The June 2010 research update will provide more detail about which projects were chosen for funding and hopefully have more good news about our cats and sheep.

The PYR trials are underway with mixed results. The research team is currently studying the data and working on effective dosage levels and planning the next course of action.



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We are making real progress – thanks to your support!! It is not just a tag line – “The CURE is within reach”.

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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