

FINAL REPORT : American Sheep Industry Association *Let's Grow Program*
PROJECT TITLE: GM1 SHEEP PRODUCTION FOR HUNTINGTON'S DISEASE

Project Leader: Susan Holler and Mina Doerner

Organization Submitting: Dakota Lamb Growers Cooperative

Let's Grow Program Grant Awarded 12/15/2015

Project Summary

A safe, plentiful source of GM1 ganglioside for therapeutic use for clinical trials in Huntington's disease (a fatal progressive genetic neurologic disease) is needed. Prior development in the field was based on GM1 production from bovine brain collected at slaughter plants throughout Europe. In the 90's, Phase II clinical trials were in progress for spinal cord injury and Parkinson's disease when Mad Cow Disease (BSE) was diagnosed in cattle in England. With the discovery of BSE, raw material from non-source verified animals of any species could not be reliably used for ganglioside production for pharmaceutical use. GM1 ganglioside cannot be practically synthesized. GlycoScience Research Inc. (GSR) has developed a unique genetic line of sheep that has been deemed an acceptable raw material source for GM1 ganglioside production for pharmaceutical use in a recent pre-Investigational New Drug application review by the FDA. While these sheep represent the only avenue for GM1 ganglioside production, the Pharmaceutical Industry, venture capitalists and many in the National Institutes of Health are skeptical of the Sheep Industry's ability to meet demand for GM1 ganglioside. The goal of this project, funded by the American Sheep Industry Association's *Let's Grow Program*, is to spread an awareness of the GM1 project to sheep producers along with an awareness of debilitating neurologic disease, specifically HD.

The success of the GM1 for HD project relies solely on the ability of the American sheep industry to respond to the demand for GM1 ganglioside affected lambs in large numbers once the GM1 molecule has been approved for use in treating human neurologic diseases, including HD. Grassroots outreach efforts, primarily through video sources and social media, will be the best way to mobilize the industry, one producer at a time. Hopefully the videos will also enhance fundraising opportunities to raise the \$5 million estimated to be needed to proceed into FDA approval and clinical trials.

Let's Grow Program funds were used to produce a series of educational and outreach videos which were widely distributed via YouTube and social media, and regionally via flash drive content. The video presentations were designed as a series of short videos which can be viewed individually, but together present the complete history and vision of the GM1 project and emphasize the urgent need to proceed with GM1 federal approvals in order to assist Huntington's Disease (HD) patients and their families. Sound bites of certain video segments are edited to be released as short, powerful, statements in social media communications on the project and/or news outlets. The American Sheep Industry Association's *Let's Grow Program* funding support is acknowledged in each video. Funding and support information for the *Let's Grow Program* for the sound bites will be included within the post text. Flash drives all include the *Let's Grow Program* logo on one side of the case, with GSR on the reverse.

We would like to note that footage which was collected during the project but not used in the current videos can be combined at some point in the future, given additional funding, into a longer film documenting the GSR journey from concept to commercialization of the GM1 product.

Project Objectives

The outcomes of this project were very successful, resulting in 7 new educational videos (see Attachment 3; *Let's Grow Program*-funded, flash drive **video titles in red**) plus 17 edited sound bites for social media use. The *Let's Grow Program*-funded project provided travel and production expenses for Nicole Richmond to conduct on-site interviews with Susan and Larry Holler of GlycoScience Research, participating sheep producers, and HD families who desperately need a treatment. Dr. Larry Holler's presentation, "The Shepherd's Gift: GM1 for HD" presented at the Michigan Sheep Breeders Association (MSBA) annual meeting in Jan. 2016, was also recorded in its entirety by the Michigan Farm News, Michigan Farm Bureau. Additional expenses included distribution of the videos contained on flash drives, accompanied by an informational letter (see Attachment 1), a document acknowledging funding by the American Sheep Industry Association's *Let's Grow Program* (see Attachment 2), a list of criteria for joining the GM1 project (Attachment 3), and a Table of Contents with suggested order of viewing for the flash drive (Attachment 4). All videos funded by the *Let's Grow Program* contain acknowledgements and American Sheep Industry Association and *Let's Grow Program* logos within the footage, generally at the end of the segment.

Additional videos and video footage from other sources were added to the flash drives and to the YouTube library. These complete the educational video portfolio highlighting the need for GM1 in the fight against HD and include video by the Michigan Farm Bureau of Dr. Heather and Mike Ludlam. Permission to use this video footage in the GM1 project made Nicole Richmond's travel to Hopkins, Michigan unnecessary. The funds originally in the grant budget were used elsewhere to create original video footage of Bev Hartig, Larry and Susan Holler, and Gary Dunbar (see Table 1).

Unfortunately, weather and conflicting schedules conspired to prevent the video documentation of HD research efforts on-site at Massachusetts General Hospital/Harvard Medical School and the joint interview of Dr. Larry Holler and Dr. Steven Hersch. Using these remaining funds by permission of the *Let's Grow Program* director, Alan Culham, Susan and Larry Holler traveled to Indiana in April 2017 to accept a monetary award from The Bev Hartig Huntington's Disease Foundation (TBHHDF); their travel expenses were supported by the *Let's Grow Program* funds. Bill Crawford of Harbor Pictures recorded interviews with Bev and her husband Bob, and Larry and Susan Holler prior to the TBHHDF fundraiser. Additionally, Bill interviewed Gary Dunbar, Ph.D., a GM1 researcher at Central Michigan University with whom Larry Holler made contact with during spring of 2017. These three interviews are some of the most powerful and compelling captured for this project. The Harbor Pictures video became available too late to be included on the original distribution of videos, but *Bev Hartig: Living with Huntington's Disease since 1999* will be added to the remaining flash drives, and is posted to YouTube as well as the GlycoScience Research website. Dr. Dunbar's interview has been recorded as a collection of 17 sound bites, and will be used strategically in social media formats to promote awareness of the project.

The portion of the budget reallocated for TBHHDF travel and resulting videos is itemized below. The first invoice from Harbor Pictures for filming and editing work totaled \$1786.12. The balance of this invoice, and the final invoice for editing by Harbor Pictures, was paid from the *Let's Grow Program* grant (GM1 SHEEP PRODUCTION FOR HUNTINGTON'S DISEASE: TRAINING VIDEOS, RECORD MANAGEMENT, AND COOPERATOR COMMUNICATIONS PROJECT) awarded on 5/15/2016.

Dakota Lamb Growers Co-op has paid the vendor but not yet submitted these invoices for reimbursement from the *Let's Grow Program* funds. Bill Crawford, owner of Harbor Pictures, gave us a \$225.26 discount on the final editing of the videos he produced (see Table 2).

In the course of preparing the videos and flash drives for editing and distribution, we found that we had not anticipated how to transfer, share, and temporarily store the videos for use among the four people working on the project. We temporarily subscribed to Dropbox, which worked quite well, but cost \$75.

The video presentation, along with additional paper documentation on the GM1 project, has been distributed on forty-five USB flash drives to all participating GM1 cooperators as well as selected interested entities regionally. Since the project is currently awaiting generation of supporting data for clinical trials, and funding for these trials, a decision was made to postpone distribution of the education and outreach videos to sheep and wool producer groups until a time when the project can take on and support more sheep producers. In the meantime, we will be sending out an email to these groups with project status information and links to several, but not all, of the videos.

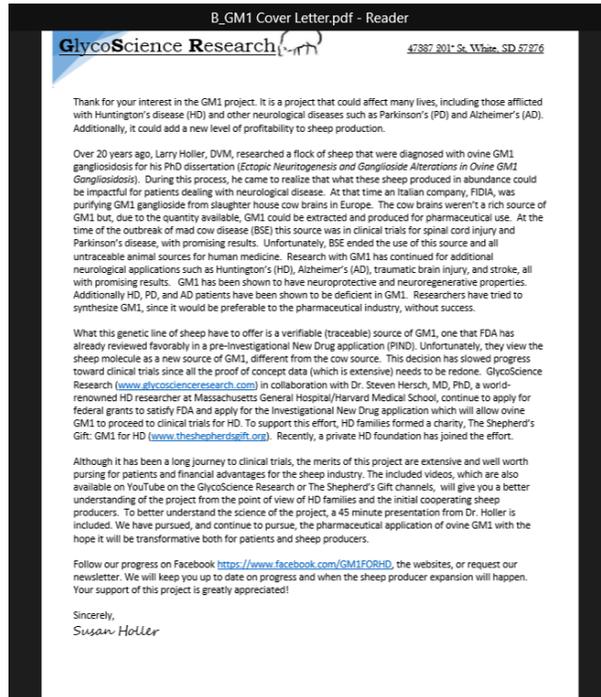
Table 1:

<u>Grant Item</u>	<u>Submitter portion</u> (see cost share amounts in table below)	<u>ASI Portion Budgeted</u>	<u>Actual Spent</u>
Travel for Interviews			
Midwest SD, ND, IA (Ms. Richmond)			
Flight to Sioux Falls, SD		\$350	\$361.70
Lodging/rental car/per diem (7 days)		\$1350	\$906.68
Hopkins, MI (Ms. Richmond)			
Mileage/lodging/per diem		\$550	\$0
Mass. General Hospital/Harvard Medical (Ms. Richmond, Dr. Holler)			
Flight/ground transportation x 2		\$1300	\$0
Lodging/per diem x 2		\$1080	\$0
Production-Nicole Richmond, Videographer			
Video, planning, production, post-production, interactive & social media consulting		\$3000	\$3000
MFB video of MI Sheep Growers presentation			
Farm Bureau Farm News Media		\$450	\$460
Travel for Bev Hartig Interviews			
Larry and Susan Holler travel		\$0	\$1422.33
Harbor Pictures Company-recording & editing			
Bev Hartig/Gary Dunbar/Hollers footage		\$0	\$1317.26
Deliverables & Distribution			
USB drives, printing, ads, postage,		\$1000	\$1612.03
TOTALS		\$9080.00	\$9080.00

Table 2:

Cost Share/In Kind Contribution	Amount
DLGC President travel (40 hrs for Midwest region interviews)	\$800.00
DLGC Manager (15 hrs for administration of grant post-award)	\$300.00
Harbor Pictures Company-in-kind donation, video editing time	\$225.26
TOTAL	\$1,325.26

ATTACHMENT 1 (note: this letter was printed on GSR letterhead; pdf could not be inserted into document.)



Thank for your interest in the GM1 project. It is a project that could affect many lives, including those afflicted with Huntington's disease (HD) and other neurological diseases such as Parkinson's (PD) and Alzheimer's (AD). Additionally, it could add a new level of profitability to sheep production.

Over 20 years ago, Larry Holler, DVM, researched a flock of sheep that were diagnosed with ovine GM1 gangliosidosis for his PhD dissertation (Ectopic Neuritogenesis and Ganglioside Alterations in Ovine GM1 Gangliosidosis). During this process, he came to realize that what these sheep produced in abundance could be impactful for patients dealing with neurological disease. At that time an Italian company, FIDIA, was purifying GM1 ganglioside from slaughter house cow brains in Europe. The cow brains weren't a rich source of GM1 but, due to the quantity available, GM1 could be extracted and produced for pharmaceutical use. At the time of the outbreak of mad cow disease (BSE) this source was in clinical trials for spinal cord injury and Parkinson's disease, with promising results. Unfortunately, BSE ended the use of this source and all untraceable animal sources for human medicine. Research with GM1 has continued for additional neurological applications such as Huntington's (HD), Alzheimer's (AD), traumatic brain injury, and stroke, all with promising results. GM1 has been shown to have neuroprotective and neuroregenerative properties. Additionally HD, PD, and AD patients have been shown to be deficient in GM1. Researchers have tried to synthesize GM1, since it would be preferable to the pharmaceutical industry, without success.

What this genetic line of sheep have to offer is a verifiable (traceable) source of GM1, one that FDA has already reviewed favorably in a pre-Investigational New Drug application (PIND). Unfortunately, they view the sheep molecule as a new source of GM1, different from the cow source. This decision has slowed progress toward clinical trials since all the proof of concept data (which is extensive) needs to be redone. GlycoScience Research (www.glycoscienceresearch.com) in collaboration with Dr. Steven

ATTACHMENT 1 (*original text continued*)

Hersch, MD, PhD, a worldrenowned HD researcher at Massachusetts General Hospital/Harvard Medical School, continue to apply for federal grants to satisfy FDA and apply for the Investigational New Drug application which will allow ovine GM1 to proceed to clinical trials for HD. To support this effort, HD families formed a charity, The Shepherd's Gift: GM1 for HD (www.theshepherdsgift.org). Recently, a private HD foundation has joined the effort.

Although it has been a long journey to clinical trials, the merits of this project are extensive and well worth pursuing for patients and financial advantages for the sheep industry. The included videos, which are also available on YouTube on the GlycoScience Research or The Shepherd's Gift channels, will give you a better understanding of the project from the point of view of HD families and the initial cooperating sheep producers. To better understand the science of the project, a 45 minute presentation from Dr. Holler is included. We have pursued, and continue to pursue, the pharmaceutical application of ovine GM1 with the hope it will be transformative both for patients and sheep producers.

Follow our progress on Facebook <https://www.facebook.com/GM1FORHD>, the websites, or request our newsletter. We will keep you up to date on progress and when the sheep producer expansion will happen. Your support of this project is greatly appreciated!

Sincerely, Susan Holler

ATTACHMENT 2

Acknowledgements GM1 Sheep Production for Huntington's Disease Project

This education and outreach project, *GM1 Sheep Production for Huntington's Disease*, would not have been possible without generous funding support awarded by the American Sheep Industry's *Let's Grow Through Change Program* funding committee. The *GM1 Sheep Production for Huntington's Disease* grant project received two rounds of funding for educational and training video production, and for the development of a record management database and a communication system for GM1 cooperators.



The Dakota Lamb Growers Cooperative supported the project with the cost-share of manager time devoted to managing the GM1 Sheep Production for Huntington's Disease grant project.



Thanks to Nicole Richmond, owner of Nicole Richmond Photography, for her work in conducting interviews, capturing footage, and producing most of the videos featured in the GM1 Sheep Production for Huntington's Disease grant project.

Thank you to Jace Bennett for assistance in Blood Sample videos and with the GM1 project.

Thank you to Brad Nupen and Aaron Cooley for creating the Oss Family video.

Thank you to Paul Fishback and Northern Voyage Productions for Katelyn Sandbulte's video.

Thank you to Michigan Farm Bureau, Inc. for granting permission to use the Heather and Mike Ludlam video.

Thank you to Bill Crawford of Harbor Pictures for donating editing time for *Bev Hartig: Living with HD*.

Thank you to Dr. Gary Dunbar, and Bev and Bob Hartig for their participation in project videos.

Thank you to the South Dakota Agricultural Heritage Museum for partial funding of the GM1 animated film.

Thank you to Cable Hardin and Gwen McCausland for creating the GM1 animated film.

Thank you to The Shepherd's Gift: GM1 for HD Board of Directors for participating in project videos and for partial funding of the GM1 animated film.

Thanks to the Huntington's Disease Families who continue to work towards a treatment for HD.

Thanks to the GM1 Project Cooperating Sheep Producers, without whom we could not meet the need for GM1.

Sincerely,
Susan and Larry Holler
GlycoScience Research, Inc.
Revised 1/2018

ATTACHMENT 3

GM1 Cooperator Information
Glycoscience Research, Inc.
GM1 Sheep Production for Huntington's Disease Project

Participation Criteria for Producing GM1 Lambs

1. Membership in Dakota Lamb Growers Cooperative (DLGC)
www.dakotalambgrowers.com or email dakotalambgrowers@gmail.com.
 - DLGC will serve as a networking and educational resource for cooperators in addition to tracking affected lambs
 - a. \$100 Membership Fee
 - b. Minimum of 50 shares (shares for sale list provided)
2. Signed GM1 Production Agreement available through DLGC
 - Lambs are expected to be delivered by 90 days of age to receiving facility

ATTACHMENT 4

**GM1 Cooperator Information
GlycoScience Research, Inc.
GM1 Sheep Production for Huntington's Disease Project**

USB Drive Table of Contents (Revised 1/2018)

- **Letter of Introduction from GlycoScience Research, Director of Operations, Susan Holler**
- **Acknowledgements**
- **Participation Requirements for GM1 Production**
- **Videos** (videos will also be available at YouTube)

<i>Video Folder Name</i>	<i>Video Title</i>	<i>Video Length (minutes)</i>
Folder: GM1 Scientific Presentation		
	Dr. Larry Holler Presentation	60.0
	GM1 Sheep Can Treat Neurologic Disease	3.1
Folder: Project Information		
	GlycoScience Research Farm Tour and History	17.2
	Bev Hartig: Living With Huntington's Disease Since 1999	6.5
Folder: Huntington's Disease Families		
	Hilton Family	9.4
	Katelyn Sandbulte	3.2
	Oss Family	7.2
Folder: Cooperating Sheep Producer Commentaries		
	Heather and Mike Ludlam	5.4
	Jeff Petersen Family	3.2
	Jim Hanssen	2.3
	Pam and Greg Taylor	9.1
Folder: Training Videos - IDs, Blood, Packaging		
	Animal Identification Options	5.5
	Blood Sample Packing Summary (pdf)	N/A
	Drawing Blood Samples (All Ages)	10.1
	Packaging Blood Samples	6.1

GM1 Sheep Production for Huntington's Disease Project

Funded by:

In cooperation with:

