MAY 2017

AMO Update

New medicines. Better lives.

Mike Snape, PhD

Welcome to AMO Update

Welcome to the first issue of AMO Update. Our new newsletter is designed to provide a wide range of insights and information about our work and our commitment to supporting individuals and families affected by many serious health issues.

All of us at AMO Pharma share a passion for drug development that is continually strengthened and inspired by many personal connections we have to the rare disease community. Within our own families, through friends and colleagues, and in our detailed research related to the new therapies we will develop, we are working to build a fuller understanding of the impact that diseases have on the lives of both patients and their entire care teams. We then use these insights to guide our clinical research and identify opportunities to support many essential efforts in disease awareness and patient and clinician education.

We are currently working on multiple promising programs in genetic disorders, including AMO-02 for the treatment of congenital myotonic dystrophy (DM1). These programs reflect our commitment to acquiring and advancing therapies with the potential to represent major advances in care in patient populations that are in desperate need of new treatment options. In this newsletter we are pleased to provide an update on the development program for AMO-02, which has recently advanced to a Phase 2 clinical trial in the U.K. for patients with early onset myotonic dystrophy.

To bring you a broad range of perspectives, we will also invite leaders from the research, treatment and patient advocacy communities to share their opinions and insights with you in the months ahead. In this issue, we are very pleased to present an update on the development program for AMO-02 from our lead investigator, Professor Hanns Lochmuller of the Institute of Genetic Medicine at Newcastle University, as well as a personal story of caring for someone with DM1 from Suzette Ison.

With the launch of AMO Update, we also invite you to share with us your suggestions for the types of information you feel will be important. Our hope is that AMO Update will be a great way for you to keep up with our news while also helping all of us better understand and appreciate the challenges individuals and families face when living with many rare and serious health issues. Hopefully, this will inspire all of us to continue in the effort to support the thousands of patients and families affected by these diseases around the world.

Sincerely

Mike Snape, PhD
Chief Executive Officer, Chief Scientific Officer
AMO Pharma, Ltd.

Myotonic Dystrophy: One Family's Story

I didn't notice that my son Billy was experiencing unusual symptoms until he was about five years old and already in preschool. By that time, he was sleeping a great deal – even at times with his eyes open. He was also having trouble learning in school. When he reached first grade and began to have writing assignments, he started to experience severe pain in his hands. Initially I thought Billy was exaggerating the pain and I tried to encourage him to complete his homework, but I began to notice that the pain was so intense that it caused him to cry and seemed unbearable.

Billy's two older sisters were more advanced in their learning and other areas when they were his age. Even though I am a nurse, I could not explain his continuing symptoms, including excessive sleepiness, difficulty with thinking and problem solving, and pain in his hands. I consulted with several different medical specialists who concluded that Billy was experiencing a mild developmental delay. They told me he would "outgrow it," noting that boys typically develop at a slower pace than girls, which would explain why his sisters had advanced at a faster rate. I continued to feel that something more serious might be occurring, and I kept searching for answers.

Suzette and Billy Ison

In my efforts, I consulted with a gastroenterologist, several neurologists, and an autism clinic, and I arranged for Billy to undergo neuropsychological testing to measure his psychological function. Our family doctor continued to feel that Billy suffered from a type of developmental delay. Another doctor mentioned that Billy may have a condition known as fragile X syndrome, the most common inherited cause of autism and intellectual disabilities. Other specialists, however, ruled out fragile X syndrome and autism, noting that Billy did not meet the criteria used to confirm patients on the autism spectrum. I continued to consult with multiple doctors, but no one seemed able to offer a conclusive diagnosis. I would often insist that I thought Billy was experiencing more than just a developmental delay, but my concerns were often dismissed. In one instance, I saw a doctor's notes in which he wrote "mother has been told it's a developmental delay."

Billy's half-sister on his father's side was diagnosed with myotonic dystrophy type 1 (DM1) at Cincinnati Children's Hospital Medical Center. Until she got this diagnosis, her mother seemed to be going through the same challenges I was facing. I asked her mother for a copy of the test results, which I took to our family doctor. The doctor ordered the same blood test for Billy, and finally at 10 years old he received an accurate diagnosis of DM1. At last we had an answer, but in many ways our work was just beginning. I immediately took him to see Dr. Richard Moxley in Rochester, New York for a second clinical opinion and to begin formulating a plan to manage this complex and complicated disease.

> "Following Billy's diagnosis, my life changed dramatically. I rearranged many aspects of my life so that I could be his caregiver and better manage his disease."
>
> — Suzette Ison

DM1 is a genetic disease characterized by muscle weakness and myotonia (delayed relaxation of muscles), heart abnormalities, cataracts and insulin resistance. Descriptions of the condition indicate that it can lead to significant physical and cognitive impairment.[1] DM1 can occur at any time, and symptoms can vary from muscle pain to serious respiratory and cardiac issues. The congenital form of DM1 is the most severe form, with symptoms that can be life-threatening.[1] There is no treatment for DM1, and it seemed clear that Billy would need more care as he got older. Eventually, his father and half-brother were also diagnosed.

Following Billy's diagnosis, my life changed dramatically. I rearranged many aspects of my life so that I could be his caregiver and better manage his disease. I left my job as a full-time nurse at a local hospital to work for a company that allowed me to work from a home office, giving me more flexibility to manage his care. I take him to all his doctors' appointments, tests and other appointments. I help him every morning, evening, during all my work breaks, at lunchtime and throughout the night and on weekends. It's a 24-hour job. I make sure he's ready and

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[1] http://www.myotonic.org/what-dm/faqs

Myotonic Dystrophy: One Family's Story

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dressed in the morning and that he takes care of his service dog, Boise. Billy does need a second caregiver who helps him while I am working, but I take care of us both by myself.

Once Billy turned 18, I became his legal guardian. I will continue to make his care a priority in my life, but I often worry about what will happen when I pass away. To prepare for the future, I set up a special needs trust fund for Billy. My eldest daughter and son-in-law, who live next door, will be his legal guardians when I'm gone. A few years ago, I bought the land next door to them and built a house customized for Billy that is handicap accessible and has a roommate-type floor plan. This could help Billy live independently while still being next door to family. If his health declines, he also could transition to live with my eldest daughter and son-in-law.

Until then, Billy, who is now 22 years old, is working so hard to remain as independent as he can. He hasn't passed his driver's test yet, but he does drive his John Deere Gator tractor on our land with his service dog. This allows him the freedom to drive – even if it's just on our property. He participates in a bowling team each week, volunteers at a local humane society, and will hopefully find a part time job on weekends.

Billy's ongoing symptoms include excessive sleeping, cognitive impairment and learning disability, trouble with executive decision-making and chronic gastrointestinal symptoms. He developed pain in his neck and head caused by weakened neck muscles, so I bought him a neck brace to help hold his head up. He is ambulatory, but tires easily, especially when walking long distances. I bought him a manual wheelchair so I can push him when we are walking long distances. Billy also experienced heart episodes in a recent heart study, but our cardiologist does not feel that they are severe enough to require a pacemaker yet. He has had episodes of atrial fibrillation requiring cardioversion, and subsequently cardioverted back to a normal sinus rhythm. The only medications he uses are Imodium and Tylenol rarely for his pain; he refuses to take any stronger pain medication. He took mexiletine for his severe hand myotonia, but said that it didn't work. While there is still no approved treatment for DM1, I continually look for clinical research studies that might be appropriate for him. I know that we will not find an effective treatment by standing by and watching and hoping; we have to make it happen.

As a caregiver, managing DM1 can be isolating. You continually feel that no one can truly understand your experience – except another DM1 caregiver. It's an entirely different world. There are many times where I struggle to get through the day. I have always been very active in the DM1 community, and this has helped tremendously. I have connected with and learned from other families who understand the challenges we all face. I also attend as many medical conferences as I can to learn about advances in research and talk with friends and families that are also dealing with DM1. I started the first DM1 support group in Indiana after Billy's diagnosis, to help build a stronger community of support. I also volunteer with the Myotonic Dystrophy Foundation (MDF) and recently spoke to the U.S. Food and Drug Administration in Maryland about DM1. I advocate for the DM1 community every year on Capitol Hill. Before the MDF was created, I traveled to California each year to be a part of The Myotonic Dystrophy Assistance and Awareness Support Group and also traveled to Capitol Hill and advocated with Parent Project Muscular Dystrophy. Through these efforts, I want more people to understand that people living with DM1 are not lazy – their symptoms make them very tired and very weak. There is a desperate need for compassion and support, and we must not stop until there is an effective treatment.

Billy on a visit to Capitol Hill

I normally am a passive and quiet person, but having a son with DM1 has forced me to become a public advocate to ensure that he and others affected by this terrible condition have the services and support they need to face the future. Due to his cognitive impairment, Billy cannot advocate for himself or fully understand his disease and how DM1 progresses, so for the rest of my life I will advocate for him and for other families.

If you would like to share your story, please contact us at Sara@amo-pharma.com.

Professor Hanns Lochmuller
Institute of Genetics
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AMO-02 Trial for Myotonic Dystrophy in the UK...

The AMO Pharma Phase 2 clinical trial in the UK is working to assess the benefits of treatment with the investigational therapy AMO-02 (tideglusib) in adults with congenital and childhood onset myotonic dystrophy. As the first sponsor-led clinical study in this population, it represents an historic milestone in research and a new era of hope for patients and their families. In addition to advancing the development of AMO-02, this study will provide many new insights to help us plan for future research. The entire research community remains very excited about this program and the prospect of a future of improved health for people living with myotonic dystrophy.

... and Regulatory Progress

AMO Pharma is currently conducting an initial clinical study in adults with congenital or childhood onset myotonic dystrophy. AMO-02 reverses abnormal enzyme activity caused by the genetic change in myotonic dystrophy – by doing this AMO-02 potentially establishes normal tissue development. This study is taking place at a single site at Newcastle in the UK. The data we obtain from this study will enable us to determine whether AMO-02 is generally safe and well tolerated, and will give the opportunity to determine whether further studies are justified. In preparation for potential future studies, AMO Pharma has engaged with the regulatory teams at the U.S. Food and Drug Administration (FDA), who have accepted our Investigative New Drug Application for AMO-02, granting us authorization to conduct a clinical study in the U.S. in the future. The FDA has also granted Fast Track status for this program. Fast Track designation is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions that have the potential to fill unmet medical needs. Pending completion of our review of the data from our currently ongoing study, we will provide an update on plans for the further development of AMO-02 in our next newsletter.

Patient Resources for Information and Support

Many organizations offer information and support to patients and their families:

Myotonic Dystrophy Foundation
http://www.myotonic.org

Muscular Dystrophy Association
http://www.mda.org

Muscular Dystrophy UK
www.musculardystrophyuk.org/about-muscle-wasting-conditions/myotonic-dystrophy

In addition, many countries now have patient registries for myotonic dystrophy. For additional information on resources and to access a DM1 family and patient registry, please visit: https://myotonicregistry.patientcrossroads.org

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