

A man wearing a flat cap, glasses, a plaid jacket, and dark trousers is sitting on a rocky beach. He is holding a small, scruffy, light-colored dog. The background shows the ocean and a coastline under a clear sky.

More than hope. Progress.

“ If I look back on 2017, this is the brightest spot for people with progressive MS. And let’s face it: People living with primary- or secondary-progressive MS haven’t seen much more than a flicker from the research world **until now.**”

– Trevis, living with MS since 2001, Ireland

2017 REPORT OF PROGRESS

INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS

FUELING PROGRESS, AWARENESS, UNDERSTANDING AND COLLABORATION

Ending progressive multiple sclerosis (MS) is an urgent and unmet worldwide need. People living with this form of MS face uncertainty, losing ground each day as they experience worsening symptoms, which can cause a sense of helplessness. MS, a complex, degenerative, neurological disease, has an enormous health and social impact on an estimated 2.3 million people worldwide living with the disease. They experience debilitating symptoms including fatigue, pain, difficulty walking, and decreasing ability to work and function independently. The global burden of MS exceeds €205 billion annually.

Approximately, 65 percent of those with MS live with a progressive form, for which there are limited treatment options. Today, there is one approved therapy for primary progressive MS, but there is no treatment for secondary progressive MS. Additionally, those with relapsing MS face the possibility of their disease converting to secondary progressive MS which can lead to permanent paralysis, compromised cognition, and complications. This includes spasticity, difficulty swallowing, speech problems, and personal care issues that can require assisted living. Individuals with progressive MS experience loss every day; this uncertainty about the future can cause depression, anxiety, and a deepening sense of hopelessness.

The emergence of a therapy for primary progressive MS in 2017 is very exciting, but this single treatment option is effective only for some. As with the first treatments for relapsing-remitting MS that changed and accelerated the landscape of MS treatment development, we must seize on the momentum of this first treatment approval for progressive MS to ensure the more rapid development of additional treatments for progressive MS.

More must be done so that EVERYONE has an effective MS treatment. The International Progressive MS Alliance (Alliance) is ensuring that more will be done, fueling awareness, understanding and research collaboration. **People living with progressive MS now have hope for the future.**



“ What upsets me about MS is that it’s constantly changing, that you don’t know what cards you’re dealt with, hour to hour really. And it’s always taking away, you never get anything back.

It’s always disappearing.”

– **Laura**

Living with MS since 1995,
U.S.

AN UNPRECEDENTED GLOBAL EFFORT

The Alliance is an unprecedented global collaboration of MS organisations, researchers, clinicians, pharmaceutical companies, trusts, foundations and people affected by progressive MS, working together to transform the landscape of multiple sclerosis. The Alliance continues to raise the profile and highlight the unmet needs of progressive MS, rallying the global community to come together and find solutions.

MANAGING MEMBERS



MEMBERS



TRUST AND FOUNDATION MEMBERS



- The Al Otaiba Family
- The Alan Buegeleisen Fund
- The Avidan Family Charitable Trust
- The Chesney Miles Charitable Fund
- Cathy and Bill Onufrychuk
- Dean Smith on behalf of FUMS
- Dick and Robin Kelly Foundation
- In memory of Georg Bruun on behalf of the Bruun Family and CP ApS
- Jim Tidwell MS Memorial Research Fund
- M&H Schwartz Family Foundation
- Yellow Rose Gala Foundation

INDUSTRY FORUM

- Biogen
- EMD Serono
- Genentech, a member of Roche
- MedDay Pharmaceuticals
- Novartis AG
- Sanofi Genzyme
- Teva Pharmaceuticals

RALLYING THE INTERNATIONAL MS COMMUNITY

Progressive MS is a complex disease that cannot be solved in isolation. We must work together to transform the MS landscape.

Through the Alliance, MS organisations world-wide have been rallying the international MS community to find new treatments for progressive MS since 2014. The sustained role of MS organisations and people affected by progressive MS assures the work remains on track and motivates scientific and industry partners to remain focused and persistent, aligning important research activities around the world to establish a coherent body of progressive MS knowledge and work that will find solutions as quickly as possible.

This comprehensive and innovative approach continues to have impact, ensuring that promising research is funded so treatments can be most rapidly discovered and developed. The Alliance has been recognized as a model approach that should be applied to other diseases—wonderful recognition that we are on the right track as we continually refine our cutting-edge approach.

In 2017, we have been reflecting on progress and evaluating the Alliance’s research strategy and next phase of work. This process was inspired by the recognition that while much has been accomplished by the Alliance, more is needed to sustain momentum.

The MS movement is united in identifying approved treatments and effective interventions for progressive MS as quickly as possible.

Please join us. Together, we have a unique opportunity to expand our global movement, remove barriers and accelerate progress for people with progressive MS.



A handwritten signature in black ink that reads "Cyndi Zagieboylo".

Cyndi Zagieboylo

Alliance Executive Committee Chair
National MS Society President & CEO, U.S.

LEADING THE PROGRESSIVE MS RESEARCH COMMUNITY INTO THE FUTURE

The Alliance has effectively focused scientific and clinical attention on solving progressive MS. It started with the knowledge, and belief, that research on progressive MS is well underway. By enabling the development of new tools and methods to streamline drug discovery and accelerating the testing of potential treatments, the Alliance is delivering hope.

Since its creation, the Alliance has stimulated and encouraged promising research worldwide to overcome existing barriers to the development of new treatments for progressive MS. The scientific, clinical, biotech, pharmaceutical, and, most importantly, MS communities have been energized to speed the development of effective disease modifying and symptom management therapies.

While the Alliance's strategic agenda has had demonstrable impact through thought leadership, convening activities, research collaborations, funding, and engagement of people affected by progressive MS in the research process, we must be relentless in our efforts. It is critical that the Alliance remains focused on our priorities to enable new treatment discovery, while reducing the time and cost of testing potential treatments. This will accelerate access to treatments for people with progressive MS.

For progressive MS, the drug pipeline of treatments in phase I and phase II clinical trials is insufficient. Many avenues must be pursued at once because there is a very high failure rate in drug development in general. We will focus our efforts on filling the drug development pipeline, balancing discovery programs and tool development by:

- Broadening and deepening knowledge about the biological mechanisms of progression
- Developing the tools for shorter clinical trials
- Focusing the rehabilitation and wellness field to develop programs and strategies that can improve quality of life

We look forward to continuing to lead important work in this area and to collaborate with other initiatives in the field. The Alliance is striving to serve the more than one million people who lose movement, freedom, and their futures to progressive MS. The benefit of solving this insidious disease will be both immediate and long-term.

The Alliance has inspired hope and expectation of progress. We must deliver—together, we can deliver faster.



A handwritten signature in black ink that reads "Alan J. Thompson". The signature is written in a cursive, flowing style.

Professor Alan J. Thompson, MD
Alliance Scientific Steering Committee Chair
University College, London, Faculty of Brain Sciences, U.K.

2017 PROGRESS IN MS RESEARCH

Since 2014, the Alliance has made global research investments through Challenge Awards and Collaborative Network Awards and we are aiming to continue to expand the landscape of progressive MS research by developing new tools and methods to streamline drug discovery. Remaining focused on our priorities will increase discoveries, while reducing the time and cost of testing potential treatments. A pathway to treatments for progressive MS is emerging.

In short time, the Alliance has demonstrated the capacity to execute plans and deliver results. Its strong and growing collaboration has created momentum in the global scientific community and built on the demonstrated success of MS organisations to identify treatments and move them to shorter, faster trials that measure patient outcomes and develop new therapies.

Awareness of progressive MS has risen beyond expectations via peer reviewed research papers, editorials, and reviews, including in the high impact journal, *Lancet Neurology*, as well as the *Multiple Sclerosis Journal* and *Nature*. The Alliance sponsors scientific summits, Industry Forum meetings, and presentations during scientific MS meetings such as the European Committee for Treatment and Research in MS, Americas Committee for Treatment and Research in MS and American Academy of Neurology meetings.

“ If you want to do something, you try your best to do it and you don't give up. I know there are a lot of people—researchers and doctors—trying very hard to find a cure for this disease, and I believe that someday, there will be help.”

– Jack

Living with MS since 1992,
Canada



COLLABORATIVE NETWORK AWARDS

The Alliance-funded Collaborative Network Awards are multi-year grants that are fueling international networks of researchers and institutions, working together to make crucial breakthroughs in understanding and treating progressive MS. The work of the Collaborative Networks began in 2017 and updates on these three projects are as follows:

DRUG DISCOVERY/ TARGET DISCOVERY/VALIDATION

Project Title: Development of a drug discovery pipeline for progressive MS

Principal Investigator: Francisco Quintana, PhD, Brigham and Women's Hospital (U.S) in collaboration with eight investigators from the United States, Canada, Israel and Sanofi Genzyme



The goal of Francisco Quintana, PhD's project is to identify drug candidates that may be effective therapies for progressive MS. The project's central idea is that targeting the innate immune system in the central nervous system will uncover effective therapeutic approaches for progressive MS. While the innate immune system normally functions to protect the body from infections, Dr. Quintana and others have found that innate immune cells in the central nervous system promote disease activity in MS and other diseases. To date, Dr. Quintana's Network team have been examining enzymes in a cell signaling pathway that are the target of the drug miglustat and are potentially druggable targets to block the destructive properties of some innate immune cells. The team is also evaluating miglustat in cells and considering a clinical trial to administer miglustat and examine the cerebrospinal fluid.

They have completed testing of 500 compounds that can penetrate the blood-brain barrier—and identified an additional compound,

which mediates signaling between different cells—for further investigation. Subsequently, they have commenced testing an additional 3,000 molecules.

Project Title: Bioinformatics and cell reprogramming to develop an in vitro platform to discover new drugs for progressive multiple sclerosis (BRAVEinMS)

Principal Investigator: Gianvito Martino, MD, Division of Neuroscience, San Raffaele Hospital Milan (Italy) in collaboration with 13 investigators from Italy, France, Germany, Europe, Canada and the United States



The BRAVEinMS team are using bioinformatics and cell reprogramming to develop an in vitro platform (for example, in culture dishes) to discover new drugs for progressive multiple sclerosis and are working to identify molecules that may have a protective role in nerve cells or neurons and/or the capacity to promote myelin repair.

The BRAVEinMS team is focusing their efforts in three phases: 1) identifying potential drugs or compounds, 2) screening these compounds for their ability to protect nerve cells or promote myelin repair in laboratory tests, and 3) evaluating candidate compounds in animal models of progressive MS. In the study's first phase, the researchers will leverage their world-class IT expertise to comb through large data sets of biological and chemical information. The short-term goals for this project are to have a definitive list of molecules that can be tested in mice using new procedures being developed by the Martino team. Then, the team will test neurons and oligodendrocytes derived from hiPSCs (human induced pluripotent stem cells). In 2018, the team expects to develop outcome measures

to best evaluate the results of the assays. Martino's team believes that BRAVEinMS will pinpoint previously unidentified molecules with a high chance of therapeutic efficacy in progressive MS patients.

Over the past year, Drs. Quintana and Martino have formed strong collaborative linkages between teams and will be coordinating their drug discovery efforts as their projects move forward.

BIOMARKERS— BIOLOGICAL/IMAGING

Project Title: Identifying a biomarker of disability progression for use in clinical trials

Principal Investigator:
Douglas Arnold, MD,
McGill University (Canada)
in collaboration with 16
investigators from The
Netherlands, United Kingdom,
United States, and Switzerland



Douglas Arnold, MD of McGill University is developing the next generation of tools for measuring disease progression in progressive MS by pioneering the development of magnetic

resonance imaging (MRI) markers that signal disease progression and adapting these for use in early (phase II) clinical trials of progressive MS treatments. Dr. Arnold's research examines the underlying idea that brain injury-associated disease progression in MS is detectable by MRI prior to its identification by physicians in a clinic visit.

Using data from previously completed clinical trials, including existing data from more than 2,000 patients and 40,000 MRI scans, the group has been working on developing machine learning tools (also known as artificial intelligence) to automatically predict future disease activity from images acquired from Relapsing Remitting MS (RRMS) patients. Although they have been focusing on RRMS patients for now, the machine learning tools they are developing will be transferable to the context of progressive MS patient images. They have been asking whether new lesions seen on MRI might predict future disease activity or changes in EDSS scores. Their team has also been creating computer tools to share and control quality of the data they are generating. Finally, the team is in discussions to add more images (equaling more data) to their database which will help in developing even more robust algorithms.

**40 LEADING
INVESTIGATORS**

3 €4 MILLION
Collaborative Network
Award grants for a
**TOTAL INVESTMENT OF
€12 MILLION**

The Alliance awarded

**ESSENTIAL,
FIRST-OF-ITS KIND
GLOBAL RESEARCH
NETWORKS**

from 21 institutions in:

- Canada
- France
- Germany
- Israel
- Italy
- The Netherlands
- Switzerland
- United Kingdom
- United States

We are engaging the

BEST EXPERTS
to lay the groundwork over
the next 4 years for
**NEW TREATMENTS AND
CLINICAL TRIALS**

Projects aim to

**REDUCE THE TIME
AND COST**
of getting therapies ready for
clinical trials, with
KEY MILESTONES

ALLIANCE INDUSTRY FORUM

Industry's collaborative partnership with the Alliance is managed through the Industry Forum and is led by Co-Chairs, Prof. Giancarlo Comi, MD, Director of the Department of Neurology, Scientific Institute San Raffaele and Bruno Musch, MD, PhD, Medical Director US Medical Affairs Neurosciences, Genentech, Inc.

- The Industry Forum ensures pharmaceutical and biotechnology companies are engaged to help inform and accelerate progress.
- Leading MS pharmaceutical and biotech companies have been working together on a shared agenda to address progressive MS and have established focus areas in order to break down barriers, including a focus on translational pathophysiology of progressive MS and data sharing.
- Industry Forum members, regulatory authorities, the Scientific Steering Committee and the Collaborative Network Award investigators met in Washington, D.C. and London in 2017.
- Industry has engaged with key regulatory authorities, including the Food and Drug Administration, Health Canada and European Medicines Agency in a continuing dialogue in MS drug development.
- Industry leadership has contributed to the development of the Alliance's future research planning, served on Collaborative Network Award Oversight Committees, and coordinated on a shared agenda for regulatory engagement.
- Industry Forum collaborators include Biogen, EMD Serono; Genentech, a member of Roche; Sanofi Genzyme; MedDay Pharmaceuticals; Novartis AG; and Teva.

- Industry is critical in helping the Alliance fulfill its goals. Their extensive knowledge of drug discovery and development, including clinical trials, and their willingness to contribute resources and financial investment will also accelerate progress.

EXPANDING ALLIANCE MEMBERSHIP

New Alliance members in 2017:

- Neuroliitto (Finland)
- The Chesney Miles Charitable Fund
- Dick and Robin Kelly Foundation
- The Al Otaiba Family

IMPORTANT ALLIANCE ENGAGEMENT ACTIVITIES, PUBLICATIONS AND PRESENTATIONS

- 13 scientific publications and 20 meeting abstracts generated from Challenge Award research.
- The Collaborative Network teams led by Dr. Francisco Quintana, Dr. Doug Arnold and Dr. Gianvito Martino's published several papers, including the highly regarded scientific journal *Nature*.
- The work of the three Collaborative Networks was featured in a Hot Topics session at the 2017 meeting of the European Committee on Treatments in MS (ECTRIMS). This meeting is the world's largest MS research meeting and brings together close to 10,000 delegates.
- The Alliance hosted two webcasts from Harvard (Boston, MA) and ECTRIMS/ACTRIMS (Paris, FR). These webinars

featured Dr. Tim Coetzee; Scientific Steering Committee Members impacted by MS, Caroline Sincock and Jon Strum; and, Alliance Collaborative Network lead researchers Dr. Douglas Arnold, MD, McGill University (Canada); Dr. Gianvito Martino, San Raffaele Scientific Institute, Milan (Italy); and, Dr. Francisco Quintana (U.S.) from Harvard University/Brigham and Women's Hospital. These webinars covered the three network projects and how more than 40 leading researchers from 21 institutions in Canada, France, Germany, Israel, Italy, The Netherlands, Switzerland, United Kingdom, and United States are working together to reduce the time and cost of getting therapies ready for clinical trials.

- Members of the Scientific Steering Committee—Alexis Donnelly and Caroline Sincock—assisted the European Medicines Agency on a number of engagements, putting across the perspective of people affected by progressive MS. Jon Strum launched the “RealTalk MS” podcast in 2017, covering an array of topics, including the Alliance and progressive MS.

- Prof. Alan J. Thompson, MD, Dean of the University College of London Faculty of Brain Sciences and Alliance Scientific Steering Committee Chair, was chosen by a committee of his peers to receive the American Academy of Neurology/National MS Society's 2017 John Dystel Prize for Multiple Sclerosis Research. Professor Thompson was honored for pioneering research in ways to address symptoms and improve quality of life for people with MS, and as a leader and driver of the Alliance.
- Prof. Per Soelberg Sorensen, MD, DMSc, Head of MS Research Unit Curriculum Vitae (Denmark) and Alliance Scientific Steering Committee member, received the MS International Federation's Charcot Award for his leadership in MS research.
- Leaders in progressive MS research met in Rome in March 2017 under the auspices of theECTRIMS and the Alliance. *MS Journal* released a special issue that featured papers stemmed from the meeting. The Alliance andECTRIMS provided sponsorship funding to allow open access to these papers.



The Alliance hosted two webcasts to discuss the three Collaborative Network projects and how leading researchers from 21 institutions are working together to reduce the time and cost of getting therapies ready for clinical trials.

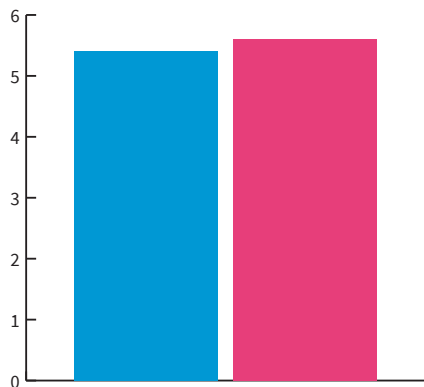
FY2017 FINANCIAL HIGHLIGHTS

The Alliance continues to exceed budgeted revenue because of growing membership and financial contributions. The Alliance has had a demonstrable impact on progressive MS in thought leadership, convening activities, collaborations and funding.

- Budgeted revenue: €5.4 million
- Actual revenue: €5.6 million
- Budgeted expenses: €2.9 million
- Actual expenses: €1.4 million

REVENUE

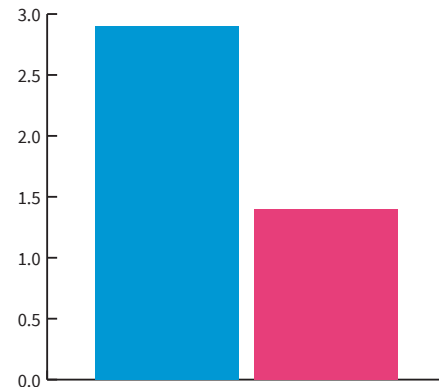
€ MILLIONS



- Budgeted revenue: €5.4 million
- Actual revenue: €5.6 million

EXPENSES

€ MILLIONS



- Budgeted expenses: €2.9 million
- Actual expenses: €1.4 million



Alliance Executive Committee leadership, pictured left to right, from the front: Cyndi Zagieboylo, CEO & President, National MS Society (U.S.); Michelle Mitchell, CEO, MS Society U.K.; Peer Baneke, CEO, MS International Federation; Klaus Høm, CEO, Scleroseforeningen (Denmark); Mario Battaglia, CEO, Associazione Italiana Sclerosi Multipla and President, Italian MS Foundation (Italy); Matthew Miles, CEO, MS Research Australia; and, Pamela Valentine, CEO, MS Society of Canada (not pictured)

The International Progressive MS Alliance.
Raising the profile — focusing the community — aligning global effort.

More than hope. Progress.



“I need the research to do more for progressive MS, like mine.”
— Cinzia, living with MS since 2011, Italy



“We don’t seem to be the forgotten group anymore—and that helps.”
— Mitch, living with MS since 2001, U.S.

Louise, living with MS since 1997, Denmark

Brian, living with MS since 2005, Canada

Ina, living with MS, The Netherlands

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