

A woman with short brown hair, wearing a black leather jacket, a grey scarf, and a yellow and purple scarf, is sitting in a wheelchair. She is smiling and looking towards the camera. The background shows a city street with buildings and a fence.

More than hope.
Progress.

2016 REPORT OF PROGRESS

MANUELA, LIVING WITH PROGRESSIVE MS SINCE 2003, GERMANY

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 debilitating form of MS face uncertainty, losing ground each day as they experience worsening symptoms, which can cause a sense of helplessness. Recently, there has been progress with the emergence of potential therapies for progressive disease, but they will be effective only for some. More must be done so that EVERYONE has an effective treatment available.

The International Progressive MS Alliance (Alliance) is ensuring that more will be done, fueling awareness, understanding and research collaboration. People with the progressive disease now have hope for the future.

Worldwide, 2.3 million people live with MS, a complex, immune-mediated, degenerative neurological disease which attacks the brain and spinal cord. There are two forms of MS — relapsing MS and a more progressive form. Those with relapsing MS face the daily uncertainty of their disease converting to a progressive form.

AN UNPRECEDENTED GLOBAL EFFORT

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

MANAGING MEMBERS



un mondo
libero dalla SM

MEMBERS



TRUST AND FOUNDATION MEMBERS



The Alan Buegeleisen Fund
The Avidan Family Charitable Trust
Dean Smith on behalf of FUMS
Cathy and Bill Onufrychuk
In memory of Georg Bruun on behalf of the Bruun Family and CP ApS
M&H Schwartz Family Foundation
Yellow Rose Gala Foundation

INDUSTRY FORUM

EMD Serono
Genentech, a member of Roche
Novartis AG
Sanofi Genzyme
Teva

STRATEGIC PRIORITIES

MS has enormous health and social impacts on those with the disease, and millions of family members and others who love and care about those living with progressive MS. Decreased mobility and pain and significant loss of cognitive function can affect people's ability to remain independent and even do the work they love. The financial impact of MS, which is most marked in those with progressive MS, exceeds €235 billion annually worldwide.

While there are several disease modifying therapies available for relapsing MS, only a few potential therapies have emerged for people living with progressive MS. The complexity of MS, and the experience gained treating relapsing MS over the past 20 years with existing therapies, strongly suggests that no single progressive MS therapy will be effective for everyone. We must continue to accelerate progress so that **everyone** affected by progressive MS will have the highly effective treatment available for their needs.

In 2016, the Alliance achieved key milestones toward new treatments in progressive MS, where we accelerate the work to deliver not just hope to people living with progressive MS, but true progress. In an unprecedented global effort to end progressive MS, the Alliance awarded three €4 million Collaborative Network Award grants for a total investment of €12 million toward accelerating the pace of progressive MS research.

The Alliance is a passionate, creative and collaborative group of thought leaders and scientific experts dedicated to doing whatever it takes to finding answers 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.

RESEARCH PRIORITIES

We are drawing the MS community together and aligning important research activities around the world to establish a body of progressive MS knowledge and work that will find solutions faster. The Alliance is focused on leveraging that knowledge, understanding what barriers must be addressed, and then funding the best research to deliver the most promising therapies. The strategy includes the development of collaborative global research networks that will speed drug development and other research toward new therapies.

Emerging therapies have the potential to improve the quality of life for some people with progressive disease; but effective treatments for everyone must be accelerated. Finding treatments in progressive MS is particularly difficult due to significantly variable and unpredictable symptoms from person to person. This variability increases the difficulty in identifying vital biological markers of progression, preventing identification of treatment targets. Without clear progression measurements, clinical trials in progressive MS have been hindered. The Alliance is ensuring that these barriers are not only addressed, but benefit from global collaboration to move this vital work forward.

The Alliance's role in bringing together all necessary stakeholders in a focused collaborative effort is crucial. This comprehensive approach has already had impact, ensuring that the most promising research is funded so that treatments can be more rapidly discovered and developed. This innovative approach has already been recognized as one to be replicated, beyond progressive MS to other diseases affecting millions more.



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.

2016 PROGRESS IN MS RESEARCH

To date, the Alliance has committed €23 million in cumulative global research investments. Through the **Challenge Awards** and the **Collaborative Network Awards**, the Alliance is generating knowledge to find new treatments for progressive MS. The inability to rapidly test potential treatments must be overcome. Without the knowledge to understand how the disease can be stopped and repaired, and without markers of progression that can be tested against treatment effects, people will continue experiencing loss of function.

The Alliance aims to change the landscape of progressive MS more quickly by developing new tools and methods to streamline drug discovery. Remaining focused on our priorities will enable new treatment discovery, while reducing the time and cost of testing potential treatments. This, in turn, will accelerate access to treatment for people with progressive MS.



Researchers from around the globe came together in 2016 for the Second Scientific Congress in San Francisco, CA.

RESEARCH HIGHLIGHTS FROM THE CHALLENGE AWARDS

The Alliance awarded 22 awards of €75,000 in 2014, designed to improve understanding of genetic and biological processes, repurpose existing drugs and speed clinical trials.

Some highlights of research progress in 2016 include:

Can the degree of meningeal inflammation and cortical pathology be used to stratify early progressive MS patients?

Lead Researcher – Massamiliano Calabrese, University of Verona, Italy

This large scale pathophysiology project analyzed cerebrospinal fluid (CSF) in an attempt to correlate CSF changes with cortical injury in MS patients. Findings could lead to the development of biomarkers for MS.

Novel infrastructure to enable monitoring of outcomes: real-time remote system to assess disability in progressive multiple sclerosis

Lead Researcher – Paul Matthews, Imperial College London, U.K.

Using actigraph technology, which is a non-invasive method of monitoring human rest/activity cycles, this data-sharing study evaluated real time assessment of gait and walking speed and could be a useful tool for the progressive MS community. This research may enhance the area of health “apps”.

Intrathecal monoclonal antibody therapy progressive multiple sclerosis

Lead Researcher – Anders Svenningsson, Umeå University, Sweden

This study was a clinical trial testing an injectable administration of rituximab via the spinal canal (intrathecal) into the cerebrospinal fluid. This group showed that intrathecal administration could completely deplete peripheral B cells (part of the immune response) using a low dose of rituximab. This trial adds to understanding the role of B cells in MS and the effects of directly administering drugs into the central nervous system.

Longitudinal multicenter cervical spinal tract diffusion MRI for progressive MS

Lead Researcher – Junqian Xu, Icahn School of Medicine at Mount Sinai, New York

This data sharing study applied advanced imaging to the spinal cord and is making progress in two key areas: 1) Standardizing spinal cord imaging to measure atrophy; 2) Developing advance imaging methods of the spinal cord to understand the pathophysiology of progressive MS.

“It’s so important to continue researching the progressive forms of MS, like mine.”

– Cinzia
Living with MS since 2011, Italy



COLLABORATIVE NETWORK AWARDS

In 2016,
the Alliance
awarded

**ESSENTIAL,
FIRST-OF-ITS
KIND**

**global research
networks**

**3 – €4
MILLION**

Collaborative Network
Award grants for a
total investment of

**€12
MILLION**

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 & COST

of getting therapies ready for clinical trials,
with **key milestones** and **deliverables**

40

LEADING INVESTIGATORS

from 21 institutions in:

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

GRANT PROJECT SUMMARIES

Stopping progression, repairing the existing damage and expediting more effective drug testing in clinical trial models specific to progressive MS is crucial to change the world for people with progressive MS. We must have effective treatments for everyone — not just for some. The Alliance’s investments in groundbreaking research will enable the global research community to tackle the significant barriers and gaps in understanding progressive MS. Together, they will move more quickly to find effective treatments for millions of people and their families who will no longer have to live with the uncertainty of what tomorrow holds.

BRAVEinMS



**Lead Researcher –
Gianvito Martino, M.D.,
Department of Neurology,
Scientific Institute San
Raffaele, Italy**

This network will develop one or more drugs that will repair damage to the brain, or protect the brain from damage altogether. The four key focus areas are:

- Developing the tools necessary to create or identify molecules that have the potential to repair myelin and protect the brain from damage
- Creating a system for testing molecules for their ability to remyelinate
- Evaluating molecular ability to repair nervous system damage
- Launching clinical trials of myelin repair or protective treatments

MS Treatment Efficacy



**Lead Researcher –
Francisco Quintana, Ph.D.,
Brigham and Women's
Hospital, U.S.**

This network will identify and evaluate drugs that protect the brain from damage in progressive MS. The three key focus areas are:

- Evaluating existing drugs to determine if they work in progressive MS
- Identifying new drugs that protect the brain from damage in progressive MS
- Defining the biological pathways involved in brain damage occurs in progressive MS

MRI Predictive Testing



**Lead Researcher –
Douglas Arnold, M.D.,
McGill University,
Canada**

This network will develop and share worldwide, a test that will predict changes in the brain during MS progression and how progression affects the brain. The four key focus areas are:

- Assembling 15,000+ MRI images of people with MS into a common database
- Creating a computer program(s) of MRI images to predict indicators of progression
- Validating and testing the accuracy and reliability of the computer program in predicting progression

ALLIANCE INDUSTRY FORUM

- Industry's collaborative partnership with the Alliance is managed through the Industry Forum. The Industry Forum ensures pharmaceutical and biotechnology companies are engaged to help inform and accelerate progress.
- Industry Forum members, regulatory bodies, the Scientific Steering Committee and the Collaborative Network Award investigators met to strengthen proposals and maximize impact.
- Industry Forum collaborators include EMD Serono; Genentech, a member of Roche; Sanofi Genzyme; Novartis AG; and Teva.
- Industry is critical in helping the Alliance fulfill its goals through their ability to contribute extensive knowledge, resources and financial investment to accelerate progress ensuring the best research design to lead to the most effective clinical trials, and drug development.

EXPANDING ALLIANCE MEMBERSHIP

New Alliance members in 2016:

- Neuro Sweden
- MS Hope for a Cure; The Alan Buegeleisen Fund; The Avidan Family Charitable Trust; Dean Smith on behalf of FUMS (Fighting and Understanding MS); Cathy and Bill Onufrychuk; Yellow Rose Gala Foundation; In memory of Georg Bruun on behalf of the Bruun Family and CP ApS; and, M&H Schwartz Family joined as Foundation & Trust Members

IMPORTANT ALLIANCE ENGAGEMENT ACTIVITIES

In 2016, the Alliance raised the profile of progressive MS, inspired the scientific community, encouraged global multi-stakeholder collaboration and motivated donors to contribute to the work of the Alliance.

ALLIANCE'S SECOND SCIENTIFIC CONGRESS — MAY

More than 200 researchers, pharmaceutical companies and supporters gathered in San Francisco, California to review research progress, challenges and next steps to speed the development of therapies for progressive MS.

Among the topics discussed were:

- **What's driving progression?** Although it is not clear what causes MS, headway is being made toward understanding how the damage done to the nervous system leads to the loss of nerve cells and progressive disability.
- **Repair and recovery:** The brain naturally reacts to the damage of MS in a number of ways, such as by repairing nerve-insulating myelin, and by compensating for damage through reorganization and plasticity, where other parts of the brain take over. Participants noted that these recovery mechanisms may be enhanced to improve function in MS.
- **Clinical trials: how to push forward?** Despite the first positive results from a large-scale clinical trial in primary progressive MS (announced in fall 2015 from a trial of ocrelizumab), many agreed that more successes are needed to change the lives of people living with progressive MS.

EUROPEAN COMMITTEE FOR TREATMENT AND RESEARCH IN MS (ECTRIMS) — SEPTEMBER

During ECTRIMS, the largest MS conference in the world, scientific leaders in MS research met in London, U.K. to address the main topics signaling the path to future MS management, with one of the focuses on progressive MS research. The Alliance held a press conference and a reception for scientists, Alliance members, and prospective donors to announce the recipients of the Collaborative Network Awards.

PUBLICATIONS AND PRESENTATIONS

- 13 scientific publications and 20 meeting abstracts generated from Challenge Award research
- "Progressive MS Alliance Industry Forum: Maximizing Collective Impact to Enable Drug Development," *Trends in Pharmacological Studies*, October 2016
- "Progressive multiple sclerosis: prospects for disease therapy, repair, and restoration of function," *The Lancet Journal*, November 2016
- "Therapies: Progressive steps," *Nature*, December 2016
- Multiple presentations by Alliance Scientific Steering Committee members and Alliance research grant recipients

ENGAGING PEOPLE IMPACTED BY MS IN RESEARCH STRATEGY

The Alliance's Scientific Steering Committee put out a call for people affected by progressive MS, to help guide the scientific direction and research activities of the Alliance. The Alliance received 234 applications from 23 countries around the world. In 2016, the Alliance welcomed three new members to the Alliance Scientific Steering Committee. This talented group of people provide additional perspective to the Scientific Steering Committee and the work of the Alliance.



Caroline Sincock (U.K.)

Caroline lives in Glasgow and is a member of the U.K. MS Society's Research Network. She has secondary progressive MS. She has a biology Ph.D. and a professional career in intellectual property. Caroline has been involved with research for several years, and co-authored a paper on outcome measures in exercise studies for MS. She represented people with MS in developing local NHS neurological services, chaired a local Neurological Voices patient group and was a Board member for a local MS charity.



Alexis Donnelly (Ireland)

Alexis is a volunteer at MS-Ireland and has served on their Research Committee since 2007. He has had primary progressive MS since 1991. Alexis works part time as a computer science university lecturer at Trinity College Dublin. He has represented people with MS in the development of an Irish Clinical Trials Network. He has also represented students with disabilities in university committees and founded a small charity to advocate for their needs.



Jonathan Strum (U.S.)

Jonathan lives in California and cares for his wife, who has secondary progressive MS. Her MS progressed very rapidly after diagnosis, and he gave up work for 11 years to care for her. He has been involved with the National MS Society, and has delivered workshops and coaching with MS caregivers in Southern California. Jonathan has a communications background and previously wrote a blog for caregivers.

“ Our purpose is clear —
to speed up the development
of treatments for people with
progressive MS.”

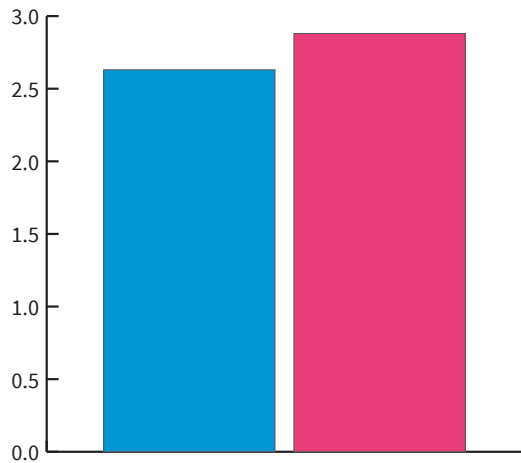
– Professor Giancarlo Comi, M.D.
Alliance Scientific Steering
Committee Vice Chair and Industry
Forum Co-Chair
Director, Department of Neurology
Scientific Institute San Raffaele, Italy

FY2016 FINANCIAL HIGHLIGHTS

For the third year in a row, the Alliance exceeded FY16 budgeted revenue as a result of growing membership and financial contributions. The Alliance has had a demonstrable impact on progressive MS in thought leadership, convening activities, collaborations and funding.

REVENUE

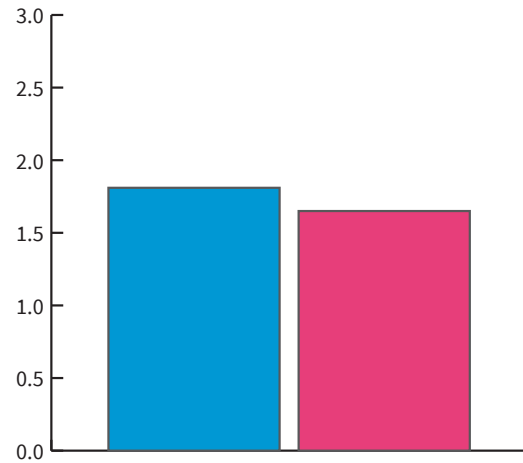
€ MILLIONS



- Budgeted revenue: €2,633,418
- Actual revenue: €2,882,434

EXPENSES

€ MILLIONS



- Budgeted expenses: €1,806,017
- Actual expenses: €1,648,205

To date, the Alliance has committed **€23 million** in cumulative global progressive MS research.

Finding solutions for EVERYONE living with progressive MS will take all of us investing in the critical next phases.

Continued urgency and additional funding is critical to accelerating progress.

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

More than hope.
Progress.



Living with progressive MS, left to right, top to bottom: William, diagnosed in 2002, U.S.; Portia, diagnosed in 1998, U.K.; Lone, diagnosed in 2006, Denmark; Kerrie, diagnosed in 2008, Australia; Maarten, diagnosed in 2007, The Netherlands.

CONTACT US TODAY

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INTERNATIONAL
PROGRESSIVE MS ALLIANCE

CONNECT TO END PROGRESSIVE MS