

MYOTUBULAR TRUST

England & Wales · Charity number 1137177

Details

Status	Registered
Legal form	Charitable company
Company number	07260229
Registered	2010-07-29
Register	View on the Charity Commission register

Contact

Address	15a Barnard Road London SW11 1QT
Phone	020 8641 6427
Email	contact@myotubulartrust.org
Website	www.myotubulartrust.org

Activities

Objects: THE RELIEF OF DISABILITY AND THE EXTENSION OF LIFE FOR BABIES, CHILDREN AND ADULTS SUFFERING FROM MYOTUBULAR MYOPATHY, BY PROMOTING THE STUDY OF, AND RESEARCH INTO, THE TREATMENT AND CARE OF THE MUSCLE WEAKNESS CAUSED BY MYOTUBULAR MYOPATHY.

Activities: The relief of disability and the extension of life for those suffering from myotubular myopathy, by promoting the study of, and research into, the treatment and cure of the muscle weakness caused by myotubular myopathy. The charity was incorporated in 2010 and the old charity number was 1113809 which should be referred to for activity up to this date.

Classification

- **How:** Makes Grants To Individuals, Makes Grants To Organisations, Provides Advocacy/advice/information, Sponsors Or Undertakes Research
- **What:** The Advancement Of Health Or Saving Of Lives, Disability
- **Who:** Children/young People, People With Disabilities

Geography

- **Area of benefit:** UNDEFINED.
- Throughout England And Wales

Finances

Period end	Income	Expenditure	Assets	Employees
2024-12-31	£138,416	£148,309	-	-
2023-12-31	£117,511	£70,876	-	-
2022-12-31	£147,462	£97,944	-	-
2021-12-31	£144,770	£112,630	-	-
2020-12-31	£132,865	£200,271	-	-

Trustees

Name	Role	Appointed
ANDREW LENNOX	Chair	
ANNE LENNOX		
James Rosling		
Lisa Bashorum		2025-10-24
PATRICIA ALLEN		2011-09-15
Zachary Richard Hughes		2025-10-24

MYOTUBULAR TRUST

England & Wales - Charity number 1137177

Accounts



Annual Report and Financial Statements

To the year ended
31 December 2024

myotubular trust
FINDING STRENGTH



UK Registered Charity, 1137177
A Company Limited By Guarantee



TRUSTEES' ANNUAL REPORT 31 December 2024

TRUSTEES' ANNUAL REPORT 31 December 2024

The Trustees of the Myotubular Trust take pleasure in presenting their annual report and the financial statements for the year ended 31 December 2024.

Objects and Activities

The objects of the Myotubular Trust as agreed by the Charity Commission are;

- the relief of disability and the extension of life for babies, children and adults suffering from myotubular myopathy
- by promoting the study of, and research into, the treatment and cure of the muscle weakness caused by myotubular myopathy.

We bring about the public benefit required of all charities, by the activities of:

- making grants to organisations and individuals
- providing support, advice, and information
- sponsoring research.

The Myotubular Trust's primary objective is to facilitate and fund medical research that advances treatments and, ultimately, help to find a cure for myotubular and centronuclear myopathy. Alongside this, the Trust provides support and information to families affected by the condition and works to enhance awareness among healthcare professionals, industry and the public.

To achieve these aims, the Trust raises funds through a combination of individual donations, corporate partnerships, grants from other Trusts and Foundations, and community-led fundraising initiatives. All activities are designed to ensure the best possible use of available resources, maximising impact for the community we serve.

Myotubular Myopathy and Centronuclear Myopathy

Myotubular myopathy is a rare and extremely life-threatening muscle condition, which causes profound muscle weakness, usually from birth. It is one of a group of conditions called **centronuclear** myopathies – under a microscope the nucleus of the muscle cell of someone affected is in the **centre**, rather than at the usual edge of the cell.

These conditions are genetic in inheritance. The gene mutation for x-linked myotubular myopathy is carried on the x chromosome (xlmtm), and is the most common form, affecting mainly boys. They usually do not survive their babyhood – the statistics have been under review in the last few years and the current view is that 50-75% die in their first year, and very few make it to adulthood. Even rarer genetic forms, either dominant or recessive in inheritance, can affect both males and females and are generally milder in severity, but not always. They usually emerge in adulthood, but again it is possible for children to be affected by these other forms. The terms myotubular and centronuclear myopathy both describe 'our' condition.

Children and adults with myotubular myopathy usually require vigilant nursing care, ventilators to breathe, power wheelchairs to get around, and are often fed via a tube into the stomach. Carrier females, and those affected by some of the rarer forms which can manifest in adult life, may develop muscle weakness and problems with eating and drinking; walking and movement; muscle fatigue and susceptibility to respiratory weakness and associated infections. It can even be fatal for a small number of seriously affected carrier women.

While myotubular myopathy has historically been considered primarily a muscle disease, and care has focused on the respiratory challenges and complications, the last five years have shone a light on liver complications too. In all three of the clinical trials myotubular myopathy (XLMTM) and centronuclear myopathy (CNM), adverse events were reported in liver

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function tests, and all three were prematurely halted for this reason. Tragically, four boys died in the gene therapy trial. A new push in our field is underway, to understand how the liver is impacted and what that means for future clinical trials and, just as importantly, for day-to-day care of all patients.

2024 – where are we now

In the 19 years since the Myotubular Trust was founded, the landscape has changed markedly. Day-to-day management of the condition has improved with evolving respiratory support techniques and, wonderfully, many children are living longer. The change in survival data is truly something to be celebrated. Substantial progress has been made in understanding myotubular and centronuclear myopathy in those 19 years, and research into a treatment, or cure, has made great steps forward, including the first human clinical trials.

However, there remain many fundamental questions about the condition, and why and how these genetic variations, and the proteins they impact, cause muscle weakness. There have been heartbreaking setbacks in the clinical trials - the gene therapy trial is still on hold after the death of four participating patients; the 'antisense' trial sponsored by the biotech start-up, Dynacure, was terminated in 2022 due to concerning liver test results; and finally, the last of the three clinical trials so far for myotubular myopathy - the repurposing of tamoxifen - had to be halted in 2024 due to serious liver adverse events. Combined with the history of some of those with XLMTM (but not all) suffering from liver complications over the years, the community now urgently needs to uncover the true natural history of the liver, and the mechanism of action by which a lack of myotubularin is implicated in the liver.

The Trust was established in 2006 by two parents of boys with myotubular myopathy, simply to raise research funds. There was such hope when, only 10 years later, the first human clinical trials began for myotubular and centronuclear myopathy, and the difficult years that have ensued since then have shown us how important it continues to be to keep these conditions at the forefront of groundbreaking research.

We are dedicated to continuing to make a meaningful difference - there is clearly a vital role for a disease specific research funder in the world of rare disease, along with a tangible need to support patients and families. We are conscious though of 'Founder syndrome' and the voice of the living patient. We aim to take every opportunity to invite in other patients, parents and families to take key roles and become leading voices in this work.

Since founding in 2006...we have:

1. Raised over **£3M**, through family-led fundraising, networks and relationships.
2. Made **19 research grants** to researchers in world class laboratories, with the support of a highly regarded Scientific Advisory Board.
3. Funded the proof of principle project for gene therapy that led to the **first ever clinical trial** for myotubular myopathy.
4. Funded **other proof of principle projects** that progressed to the only other two human clinical trials for our condition.
5. Funded research grants that contributed to the discovery of **two new genes** implicated in centronuclear and myotubular myopathy.
6. Hosted **five family conferences**, bringing together affected individuals and families, researchers, clinicians, and other health professionals, and arranged several family meetings by **Zoom both during the pandemic and beyond** with presentations from, and discussions with, global experts and scientists.
7. Created the first disease specific international **Patient Registry** to gather vital information on the condition and funded its migration to the stability and credibility of a university setting.

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8. Participated in a European Neuromuscular Centre workshop on Mouthpiece Ventilation, resulting in the publication of **MPV international best practice guidelines**.
9. Been invited on an ongoing basis by **Great Ormond Street Hospital Children's Charity** to be one of their small number of rare disease charity partners in their annual national funding call focusing on complex or rare childhood diseases.
10. Sponsored a **Standards of Care** meeting for clinicians, patients, and their healthcare professionals at the Royal Brompton Hospital.
11. Presented for LifeArc on **drug repurposing for rare diseases** and contributed to their published expert advice.
12. Contributed to the first ever **Congenital Myopathies Masterclass** for European healthcare providers. The Masterclass was organised by TREAT-NMD and included sessions led by world leading experts on myotubular and centronuclear myopathy.
13. Sponsored the UK focus group that contributed to the international study, and subsequent journal publication, **Lessons Learnt from Clinical Studies in Centronuclear Myopathies**.
14. Created a great band of **committed supporters**, raising funds for us year on year.
15. Developed strategic relationships with **key stakeholders** in the fields of neuromuscular disease, rare disease, and UK regulatory bodies
16. We co-fund research projects with highly regarded UK charities - Great Ormond Street Hospital's Charity, and the UK umbrella muscle disease charity, MDUK.
17. And *most importantly*, brought together **families** affected by myotubular and centronuclear myopathy, who support the Trust's fundraising and each other's lives.

In 2024 specifically we have:

1. Raised £138,416.
2. Continued to substantially add to our Family Factsheets, the purpose of which is to share personal family case studies to support other families in their care and decision making.
3. Invited applications for a joint grant round in partnership with Great Ormond Street Children's Charity which resulted in a grant to a team at UCL for a research project investigating the liver in XLMTM.
4. Continued our collaboration with the US patient organisation, MTM-CNM Family Connection, to run the MTM-CNM Liver Collaborative Working Group, bringing together a range of leading global experts, scientists, experienced clinicians, and biotechs, to fast-track cooperation on the understanding of liver issues emerging from current clinical trials.
5. Worked with the Myotubular and Centronuclear Myopathy Patient Registry, through the Liver Collaborative, to continue to communicate the value of a new section of academic, clinical and patient curated questions about liver health, leading to 219 patients sharing their liver data by the end of 2024 – a remarkable number for a 'new' topic for a rare disease.
6. Worked with the Registry and the Liver Collaborative to add a new set of Nutrition questions to the registry.
7. Organised a webinar for patients and families to hear directly from the research teams about the implications of the tamoxifen clinical trial being halted.
8. Continued to project manage a research team to investigate possible muscle symptoms and lived experience of xlmtm carrier women in the UK and Ireland.

Every single year since founding in 2006, we have raised 100% of our running costs separately from the funds raised by families and supporters, meaning that once again in 2024 we met our ambition to channel all the funds raised by supporters into research.

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Family Support in 2024

Advocacy and Family Support

Specific support is needed for myotubular and centronuclear myopathy patients and families, mainly because of the rarity of centronuclear and myotubular myopathy. Usually, the child's or patient's GP or doctor will never have come across the condition before - making being diagnosed a frightening and bewildering experience for all concerned. Being hurled suddenly into a world of medical jargon; high level nursing; complex healthcare and social care systems, families and individuals are grateful to know they are not alone, and that we, and others like them, are willing to share the burden of responsibility by helping them understand their experiences and how to navigate the systems.

At a time when parents are supposed to be celebrating the birth of an infant, our families are often instead in the position of having to make important choices around giving their child the best quality of life, and a chance of longer-term survival. The information these families are given by their hospital care teams to make those decisions can be patchy and possibly delivered by someone who has never seen a child with the condition before. When a baby is finally stable enough to go home, it is not unusual for the transition process from hospital to home to take 1 year to 18 months.

The need for support/information caused by a lack of understanding of the impacts of such a rare, devastatingly life threatening condition re-emerges many times throughout a patient's life – and particularly at times of change, such as when there is a physical change (such as losing the ability to walk or developing scoliosis), during periods of ill health, when moving home or into a new phase of education or work, around family planning, or practical day-to-day living issues.

In 2024 we have supported families who were:

- Applying for re-housing and needing to communicate the scale of equipment and storage needed for a growing young man with this myotubular myopathy
- Making decisions about palliative care at the point of diagnosis in a neonatal setting
- Seeking advice on the most appropriate specialist equipment for their child
- Requesting introductions to others with their own mutation and in their own age group
- Enquiring about the current status of clinical trials and future potential research
- Wanting to discuss a child's mental health at a point on life when they become aware that they are 'different' to their peers

In 2024, while providing individual support for individual issues for families, we also continued to add to **Factsheets**, our substantial repository of publicly available patient case studies and experiences that are shared in order to help improve the standards of care and quality of life of our community. We are very grateful to all the patients and families who have contributed to these case studies. They are invaluable.

The global closed Facebook group managed by Myotubular Trust – **Myotubular Myopathy** - continues to go from strength to strength, with membership reaching 950 members by the end of 2024. This group continues to provide real-time, real-life advice and perspectives for families who regularly tell us they'd be very alone without this community.

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Research in 2024

The Myotubular Trust was set up to raise funds to leverage research findings being made, and techniques being trialed, in 'more common' muscle diseases. The ultimate goal of the Trust is to invest in a diverse number of routes to a cure for all genetic forms of myotubular and centronuclear myopathy, or in treatments that alleviate the most severe symptoms. We do this by investing in the very best translational research, peer reviewed to the highest international standards, supported by an eminent Scientific Advisory Board.

The Myotubular Trust was very gratified to have provided proof of principle funding for all three of the clinical trials that came to clinic in the last 8 years.

Sadly, in 2024, the TAM4MTM clinical trial, which investigated the repurposing of tamoxifen for treating XLMTM, was discontinued due to observed impacts on liver function. This brought to an end all three of the first clinical trials for myotubular and centronuclear myopathy, as in all of them, adverse events were reported in liver function tests. Following this development, in December 2024 the Myotubular Trust hosted a webinar for the community to discuss the trial's outcomes and implications for future research.

We sincerely thank those affected by myotubular and centronuclear myopathy who took part in the trials. As one mother said, "It is one thing to live without hope, it is quite another to have hope dashed." Clinical trials, particularly for conditions as severe as ours, require enormous commitment in terms of time, travel, logistics and patience. For the trials to end makes that commitment even harder to endure, and we thank them for that endurance, and for adding to the sum knowledge of our understanding of the condition.

It is very clear that for research into a treatment for myotubular and centronuclear myopathy to progress, we need to understand more about how the liver is affected, and what goes on when there are liver complications.

Current grants

Next generation gene therapy

Dr Ana Buj Bello was the recipient of the first ever research grant from the Myotubular Trust in 2008 for her pioneering work on gene replacement therapy for xlmtm. The goal of our current grant to Dr Buj Bello and her team at Genethon is to develop an even more specific and potentially safer 'vector' to carry the missing protein, myotubularin, to muscle cells. An approach which they hope will ultimately be brought to clinical trial. They also aim to better characterise the liver in laboratory tests, both before and after gene therapy. Based on this understanding and new developments in the technology of AAV vectors, they aim to generate optimised vectors with increased potency and specificity for MTM1 gene delivery.

Studying liver disease in X-linked myotubular myopathy

Dr Jim Dowling has been the recipient of a number of research grants from the Myotubular Trust. The purpose of our current grant to Dr Dowling and his team at Sick Kids is to better understand the cause of liver disease in people living with XLMTM, and to help develop a treatment. This grant was made in partnership with the UK muscle disease charity, MDUK. We are delighted to be partnering with MDUK on this important grant, and believe it is testament to how vital it will be for myotubular myopathy, and likely many other neuromuscular conditions, to better understand the impact of gene therapy, and other treatments, on the liver in clinical trials.

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An Advanced Multi-Organoid Platform for Therapy Modelling in X-Linked Myotubular Myopathy

In 2024, as part of their annual grant call for rare paediatric disease, we partnered with Great Ormond Street Hospital Children's Charity in a three-year grant of £248,940 to Professor Francesco Saverio Tedesco and Dr. Valentina Maria Lionello at University College London. This project focuses on creating patient-specific 3D 'mini-muscles and livers' using human induced pluripotent stem cells reprogrammed from individuals with X-linked myotubular myopathy (XLMTM). These models aim to enhance our understanding of the disease and serve as platforms for testing potential gene therapies.

These liver focused grants underscore our commitment to funding and facilitating research that enhances understanding and that paves the way for effective treatments for myotubular and centronuclear myopathy.

We are immensely grateful to our Scientific Advisory Board (SAB) for their time and their expertise and understanding to bring excellence and rigor to our funding decisions. The calibre of applications the Myotubular Trust attracts is due, in no small part, to the reputation of this group of scientists.

The academic members of the SAB are:

- Professor Francesco Muntoni, Head of the Dubowitz Neuromuscular Centre, Great Ormond Street Hospital
- Dr Meriel McEntagart, Consultant Clinical Geneticist, St. George's Hospital, London
- Professor Michael Duchen, Professor of Physiology, University College London
- Dr Susan C Brown, previously Reader in Translational Medicine, Department of Veterinary Basic Science, Royal Veterinary College, University of London
- Professor Volker Straub, Harold Macmillan Professor of Medicine, Consultant in Neuromuscular Genetics and Paediatrics, Newcastle University
- Professor Dominic Wells, previously Professor in Translational Medicine, Royal Veterinary College

We are indebted for the guidance they gave to the Myotubular Trust throughout the year. We are also very grateful to the lay members of our SAB for their time. The lay members include parents, bereaved parents and patients.

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Financial Review

Achievements and Performance in 2024

In 2024 we raised £138,416 and have continued to drive forward our mission, funding key research projects, forging partnerships and growing our support network. This year, we were fortunate to receive generous grants from IGY Foundation*, Astellas Pharmaceuticals**, Global's Make Some Noise, BBC Children in Need, and Jeans for Genes. These funds played a crucial role in sustaining and expanding our work, allowing us to continue supporting cutting-edge research and vital family support initiatives. Their support means that, yet again, we have been able to commit 100% of the funds raised by families, their friends and colleagues, to research. This has been so important to us as a principle, ever since founding, and it is a source of great satisfaction that we have achieved this '100% pledge' every year for 19 years.

*A special mention goes once again to IGY Foundation who have given us so much moral and financial support over the years. Knowing how generous their philanthropy is, we fully realise there are many causes who look to them for help, and we are very grateful that they continue to value the work we do. Their support helps us to be able to meet unexpected needs from research teams and certainly helps with our running cost pledge.

**We also received a very welcome grant of £25,000 from Astellas Pharmaceuticals to support the ongoing development of the patient registry, to support for the coordination of a study of xlmtm carrier women in the UK, and to assist with the costs of organising our Hope Walks. This grant constitutes less than 18% of our 2024 income.

Community and Fundraising Activities

Our dedicated community of supporters has played an essential role in helping us raise both awareness and funds in 2024. Trust-led events included:

- The London Hope Walk, which saw over 90 walkers take to the streets and, as ever, every single one of them joined in recognition of someone with the condition. This was the 17th year of the London Hope Walk and this event over those years has raised over £250,000 – so far!
- The first-ever Manchester Hope Walk, where 70 walkers participated, representing 5 families of boys with myotubular myopathy
- Ongoing engagement with Easyfundraising – with a regularly growing number of supporters
- The growth of our regular giving programme, with new donors joining in 2024, ensuring sustained support for our work.

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In addition to Trust-led initiatives, families and supporters - across the world - undertook their own fundraising activities, demonstrating incredible commitment and creativity. Some of the inspiring events included:

- A half marathon run to raise funds, and awareness
- A surfing challenge, showcasing both endurance and spirit
- A Tough Mudder event
- A skydive in Australia in memory of a beloved brother
- Another successful Jack Blunsdon Golf Tournament – the 18th - bringing together supporters yet again for a day of fundraising on the course in memory of Jack
- A 60-mile bike ride by a devoted grandad in memory of his grandson, highlighting the personal connections that drive our supporters
- A boxing/wrestling event at the Bridge Centre, in remembrance of a special little boy
- A school fundraiser, engaging the next generation in charitable giving and awareness efforts.

We were also very grateful to the fundraisers in 2024 who applied to their company's matched funding schemes. These invaluable schemes that financially match their employees' efforts for charities are a fantastic source of funding for us.

We are also very grateful for the steady income from the supporters from whom we receive standing orders and Give as You Earn schemes during 2024. Thank you to you all.

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Fundraising Practice

The Trustees take their responsibilities to fundraising very seriously. To that end, we ensure that we adhere to the Fundraising Regulator's code of best practice and meet the Charity Commission's six principles of charity fundraising. For us, at our size, the areas of best practice we pay attention to are;

- providing information on how to fundraise safely,
- considered communication with all fundraisers, which is appropriate to our strategy,
- carrying out a proportionate process of due diligence around fund raising proposals,
- making a record of the issue and return of any charity collection materials,
- securing cash donations and banking them as soon as possible,
- not sharing personal data without explicit consent,
- including opt-out information on fundraising communications sent to a named individual,
- processing unsubscribe requests in a timely way,
- using funds as they have been directed by specific donors, in particular allocating restricted funds appropriately.

We adhere to the Data Protection Act 2018, General Data Protection Regulation (GDPR) and pay data protection fees to the Information Commissioner's Office (ICO).

Reserves Policy

The Trustees sole aim in expending cash reserves is to fund research into a cure or treatment for myotubular myopathy and they do not consider it appropriate to hold long-term reserves.

However, as each research project is granted, those funds will be held available to be released in staged payments, and new awards will only be made if the full cost of the relevant research project is available, and available to be ringfenced. This prudent financial policy is appropriate given our size and specialism.

Plans for future periods

The Trust aims in 2025 to:

- Maintain excellence in family support, advocacy, information provision – in particular our Factsheets focus - and continue to make the introductions that families tell us are invaluable.
- Organise and support Hope Walks in London and in at least one other location in the UK or Ireland.
- Actively promote and support the Liver Questionnaire and Nutrition Questionnaires on the Myotubular and Centronuclear Myopathy Patient Registry, to assist in the development of a new academic publication in time for World Muscle Society 2025.
- Promote, and fund, research that furthers our understanding of the liver and bile function in myotubular myopathy, with the goal of being able to impact both clinical trial planning and ongoing patient care.
- Continue to support the development of a UK carrier women study, building on the excellent work already being done in the Netherlands and Germany.
- Organise webinars on key topics of interest for the patient community and investigate the interest in meeting in person once again.

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- Continue to work with key stakeholders in the neuromuscular disease community, and strategic rare disease organisations.
- Continue to work with regulatory authorities on behalf of patients with myotubular and centronuclear myopathy.
- Plan ahead and prepare effectively for any future NICE review of treatments for myotubular and centronuclear myopathy, facilitating families' and patients' input.
- Continue to share information with, and promote collaboration between, other family and patient organisations, relevant scientific interest groups and research organisations.
- Continue to secure separate funding for running costs to uphold our pledge of investing 100% of funds raised by families and their networks directly to research.

Reference and administrative details of the Charity, its Trustees and advisors

The following were Trustees of the Trust and held office during the above period:

Patricia Allen
Gary Browning
Andrew Lennox
Anne Lennox
James Rosling

Trustees are appointed by the board of trustees and serve for three years (five years for Anne Lennox) after which period they may put themselves forward for re-appointment. The trustees meet three times per annum.

Office

Myotubular Trust
- charity registration number 1137177
- company registration number 07260229

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Independent Examiner

Michael Stone MA ACA
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Windsor House
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Structure, Governance and Management

Constitution

The Myotubular Trust is an incorporated charity limited by guarantee and its governing document is the memorandum and articles of association dated 21 May 2010. The memorandum and articles of association has the same objects as that of the Trust Deed dated 26 January 2006 of the unincorporated charity. The Trust obtained charitable status under Section 4 of the Charities Act 1960 from the Charity Commission on 19 April 2006 under registration number 1113809 and following incorporation on the 20th May 2010 was registered with the Charity Commission with registration number 1137177, and with Companies House with company registration number 7260229.

Organisation and the Trustees

In selecting individuals for appointment, the trustees will have regard to the skills, knowledge and experience needed for the effective administration of the charity.

Trustees' responsibilities statement

The Trustees (who are also directors of The Myotubular Trust for the purposes of company law) are responsible for preparing the Trustees' Report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards.

Company law in England and Wales requires the Trustees to prepare financial statements for each financial year in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards and applicable law). The financial statements are required by law to give a true and fair view of the state of affairs of the charity and of the income and expenditure of the charity for that period. In preparing these financial statements the trustees are required to:

- Select suitable accounting policies and then apply them consistently
- Observe the methods and principles of the Charities SORP
- Make judgments and estimates that are reasonable and prudent
- State whether applicable UK accounting standards have been followed and statements of recommended practice, subject to any departures disclosed and explained in the financial statements and
- Prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue to operate.

The trustees are responsible for keeping accounting records, which disclose with reasonable accuracy at any time the financial position of the charity and enable them to ensure that the financial statements comply with the Companies Act 2006. They are responsible for safeguarding the assets of the charity and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

Risk management

The trustees have examined the strategic, business and operational risks, which the charity faces and confirm that systems have been established to enable regular reports to be produced so that the necessary steps can be taken to lessen the risks.

INDEPENDENT EXAMINER'S REPORT FOR THE YEAR ENDED 31 DECEMBER 2024

Respective responsibilities of trustees and examiner

The trustees (who are also the directors of the company for the purpose of company law) are responsible for the preparation of the accounts. The charity's trustees consider that an audit is not required for this year under section 144 of the Charities Act 2011 (the Charities Act) and that an independent examination is needed.

Having been satisfied that the charity is not subject to audit under company law and is eligible for independent examination it is my responsibility to:

- examine the accounts under section 145 of the Charities Act,
- to follow the procedures laid down in the General Directions given by the Charity Commission (under section 145(5)(b) of the Charities Act, and
- to state whether particular matters have come to my attention.

Basis of independent examiner's statement

My examination was carried out in accordance with the General Directions given by the Charity Commission. An examination includes a review of the accounting records kept by the charity and a comparison of the accounts presented with those records. It also includes consideration of any unusual items or disclosures in the accounts, and the seeking of explanations from you as trustees concerning any such matters. The procedures undertaken do not provide all the evidence that would be required in an audit, and consequently, no opinion is given as to whether the accounts present a 'true and fair view' and the report is limited to those matters set out in the statement below.

Independent examiner's statement

In connection with my examination, no matter has come to my attention:

- 1) which gives me reasonable cause to believe that in, any material respect, the requirements:
 - to keep accounting records in accordance with section 130 of the Charities Act; and
 - to prepare accounts which accord with the accounting records and to comply with the accounting requirements of the Companies Act 2006 and with the methods and principles of the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2019) have not been met; or
- 2) to which, in my opinion, attention should be drawn in order to enable a proper understanding of the accounts to be reached.

Michael Stone

Michael Stone MA ACA
Jamieson Stone LLP
Windsor House
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W1W 8LU

17 September 2025

STATEMENT OF FINANCIAL ACTIVITIES FOR THE YEAR ENDED 31 DECEMBER 2024

	Unrestricted Funds £	Designated Funds £	Restricted Funds £	Total Funds 2024 £	Total Funds 2023 £
<u>INCOMING RESOURCES</u>					
Donations and grants	53,230	52,500	-	105,730	83,788
Fundraising activities	27,533	-	-	27,533	30,535
Interest received	5,153	-	-	5,153	3,188
Total incoming resources	85,916	52,500	-	138,416	117,511
<u>RESOURCES EXPENDED</u>					
Research	-	89,453	-	89,453	16,151
Fundraising costs	2,438	-	-	2,438	(396)
Outreach work	-	-	-	-	14
Staff costs	49,961	-	-	49,961	49,961
Training	-	103	-	103	24
Accountancy & payroll	366	-	-	366	236
Independent examiner	1,000	-	-	1,000	1,000
Legal & professional	92	-	-	92	1,262
Trustee's indemnity	1,042	-	-	1,042	1,009
Travel costs	954	-	-	954	120
Printing & stationery	-	-	-	-	25
Postage & telephone	105	-	-	105	122
Subscriptions	205	-	-	205	85
Web & IT costs	2,380	-	-	2,380	1,112
Bank charges	210	-	-	210	109
Miscellaneous costs	-	-	-	-	42
Total resources expended	58,753	89,556	-	148,309	70,876
Net incoming/(outgoing) resources	27,163	(37,056)	-	(9,893)	46,635
Transfers between funds	(37,056)	37,056	-	-	-
Net movement in funds	(9,893)	-	-	(9,893)	46,635
Total funds brought forward	18,109	405,187	-	423,296	376,661
Total funds carried forward	8,216	405,187	-	413,403	423,296

All gains and losses arising in the year are included within the statement of financial activities

The accompanying notes form part of these financial statements

BALANCE SHEET AS AT 31 DECEMBER 2024

	£	2024 £	£	2023 £
CURRENT ASSETS				
Debtors and prepayments	2,241		41,958	
Cash at bank and in hand	413,382		387,268	
	-----		-----	
Total current assets	415,623		429,226	
	-----		-----	
CREDITORS				
Amounts falling due within one year	2,220		5,930	
	-----		-----	
Net current assets		413,403		423,296
		-----		-----
NET ASSETS		413,403		423,296
		-----		-----
FUNDS OF THE CHARITY				
Restricted funds		-		-
Unrestricted general funds		14,522		18,109
Unrestricted designated funds		398,881		405,187
		-----		-----
		413,403		423,296
		-----		-----

The company is entitled to exemption from audit under Section 477 of the Companies Act 2006 for the year ended 31 December 2023 and the members have not required the company to obtain an audit of its financial statements for the year ended 31 December 2023 in accordance with Section 476 of the Companies Act 2006.

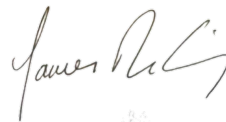
The directors acknowledge their responsibilities for: (a) ensuring that the company keeps accounting records which comply with Sections 386 and 387 of the Companies Act 2006 and (b) preparing financial statements which give a true and fair view of the state of affairs of the company as at the end of each financial year and of its profit or loss for each financial year in accordance with the requirements of Sections 394 and 395 and which otherwise comply with the requirements of the Companies Act 2006 relating to financial statements, so far as applicable to the company.

The financial statements have been prepared in accordance with the provisions of Part 15 of the Companies Act 2006 relating to small companies.

The financial statements were approved by the trustees on ..16/9/2025..... and signed on their behalf:



.....
Andrew Lennox
Chairman/Trustee



.....
James Rosling
Treasurer/Trustee

The accompanying notes form part of these financial statements

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2024

1. BASIS OF PREPARATION

The financial statements have been prepared on the accruals basis of historic cost in accordance with the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2019) and the Companies Act 2006 and the Charities Act 2011.

2. ACCOUNTING POLICIES

Incoming resources

Incoming resources are recognised when the charity becomes entitled to the resources, the trustees are virtually certain they will receive the resources, and the monetary value can be measured with sufficient reliability.

Where incoming resources have related expenditure (as with fundraising or contract income) the incoming resources and related expenditure are reported gross in the Statement of Financial Activities.

Grants and donations are recognised when the charity has unconditional entitlement to the resources.

Incoming resources from tax reclaims are recognised at the same time as the gift to which they relate.

Contractual income and performance related grants are recognized once the related goods or services have been delivered.

Investment income is included in the accounts when receivable.

Resources expended

Resources expended are recognised as soon as there is legal or constructive obligation committing the charity to pay out resources.

Resources expended include attributable VAT which cannot be recovered.

Funds

Restricted funds are funds to be used for specific purposes as declared by the donor.

Designated funds are monies set aside from general funds and designated for specific research awards by the trustees.

Unrestricted funds are donations and all other incoming resources without a specified purpose and which are available as general funds.

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED) FOR THE YEAR ENDED 31 DECEMBER 2024

3. TAXATION

The Myotubular Trust is a registered charity and is not liable to Income Tax or Corporation Tax on income derived from its charitable activities.

4. RESOURCES EXPENDED

	2024 £	2023 £
Research	89,453	16,151
Independent examiner's remuneration	1,000	1,000
	-----	-----

The principal research grants awarded during the year were as follows:

	2024 £	2023 £
Sick Kids	36,036	-
Hnia at Inserm	-	9,958
Inserm(Buj Bello) 2023-25	32,682	4,167
Great Ormond Street (GOSH)	20,735	-
Newcastle University re Treat NMD	-	2,026
	-----	-----

5. DEBTORS AND PREPAYMENTS

	2024 £	2023 £
Gift Aid	1,241	458
Prepayments and accrued income	1,000	41,500
	-----	-----
	2,241	41,958
	-----	-----

6. CREDITORS FALLING DUE WITHIN ONE YEAR

	2024 £	2023 £
Accruals	2,220	5,930
	-----	-----

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED) FOR THE YEAR ENDED 31 DECEMBER 2024

7. RELATED PARTY TRANSACTIONS

There were no related party transactions by the trustees for the year (2023: None).

One Trustee received remuneration of £20,000 during the year ending 31 December 2024 (2023: £20,000).

The trustee's remuneration and other administration costs are funded from unrestricted corporate and charitable donations, which were specifically raised for that purpose.

MYOTUBULAR TRUST

England & Wales - Charity number 1137177

Accounts



**Annual Report
and Financial Statements**

To the year ended
31 December 2023

myotubular trust
FINDING STRENGTH



UK Registered Charity, 1137177
A Company Limited By Guarantee

TRUSTEES' ANNUAL REPORT 31 December 2023

TRUSTEES' ANNUAL REPORT 31 December 2023

The Trustees of the Myotubular Trust take pleasure in presenting their annual report and the financial statements for the year ended 31 December 2023.

Objects and Activities

The objects of the Myotubular Trust as agreed by the Charity Commission are;

- the relief of disability and the extension of life for babies, children and adults suffering from myotubular myopathy
- by promoting the study of, and research into, the treatment and cure of the muscle weakness caused by myotubular myopathy.

The Trust focuses on five outcomes to enable the achievement of these objectives:

1. Bringing families together
2. Promoting and funding international research
3. Sharing knowledge
4. Promoting innovative thinking and collaboration
5. Working with our extended families.

We bring about the public benefit required of all charities, by the activities of:

- making grants to organisations and individuals
- providing support, advice, and information
- sponsoring research.

Myotubular Myopathy and Centronuclear Myopathy

Myotubular myopathy is a rare and extremely life-threatening muscle condition, which causes profound muscle weakness, usually from birth. It is one of a group of conditions called **centronuclear** myopathies – under a microscope the nucleus of the muscle cell of someone affected is in the **centre**, rather than at the usual edge of the cell.

These conditions are genetic in inheritance. The gene mutation for x-linked myotubular myopathy is carried on the x chromosome (xlmtm), and is the most common form, affecting mainly boys. They usually do not survive their babyhood – the statistics have been under review in the last few years and the current view is that 50-75% die in their first year, and very few make it to adulthood. Even rarer genetic forms, either dominant or recessive in inheritance, can affect both males and females and are generally milder in severity but not always. They usually emerge in adulthood, but again it is not uncommon for children to be affected by these other forms. The terms myotubular and centronuclear myopathy both describe 'our' condition.

Children and adults with myotubular myopathy usually require vigilant nursing care, ventilators to breathe, power wheelchairs to get around, and are often fed via a tube into the stomach. Carrier females, and those affected by some of the rarer forms which can manifest in adult life, may develop muscle weakness and problems with eating and drinking; walking and movement; muscle fatigue and susceptibility to respiratory weakness and associated infections.

While myotubular myopathy has historically been considered primarily a muscle disease, and care has focused on these respiratory challenges and complications, the last four years have shone a light on the possible liver complications that some patients may suffer from. In the first two clinical trials for XLMTM and CNM, adverse events were reported in liver function tests, and tragically there were four deaths related to the liver. A new push in our field will be needed, to understand how the liver is impacted and what that means for future clinical trials, and just as importantly for day-to-day care of all patients.

TRUSTEES' ANNUAL REPORT 31 December 2023

2023 – where are we now

In the 18 years since the Myotubular Trust was founded, the landscape has changed markedly. Day to day management of the condition has improved with evolving respiratory support techniques and, wonderfully, many children are living longer. Hence the change in survival data – something to be celebrated. Substantial progress has been made in understanding myotubular and centronuclear myopathy in those 18 years, and research into a treatment, or cure, has made great steps forward, including the first human clinical trials.

However, there remain many fundamental questions about the condition, and why and how these genetic variations, and the proteins they impact, cause muscle weakness. There have been heartbreaking setbacks in the clinical trials - the gene therapy trial is still on hold after the death of four participating patients, and the antisense trial sponsored by the biotech start-up, Dynacure, was terminated in 2022 due to concerning liver test results. Combined with the history of some of those with XLMTM (but not all) suffering from liver complications over the years, we now urgently need to uncover the true natural history of the liver, and the mechanism of action by which a lack of myotubularin is implicated in the liver.

The Trust was established in 2006 by two parents of boys with myotubular myopathy, simply to raise research funds. There was no other way for passionate parents to ring-fence money to fund research into a treatment or cure for this condition, even though we did at the time approach some larger charities for whom we had hoped to fundraise. We also realised very quickly that it was essential to support the profile of the condition within the neuromuscular research community – to compete for brains and innovative ideas – and to support those living with, and bereaved by, myotubular myopathy.

There are new understandings of the condition emerging particularly from the clinical trials, which present several new challenges, but also new avenues of research. We need to be here to voice the urgency of this work, and to be a source of funding too. We can be fleet of foot as an organisation when a fundamental new question emerges, as we were when we changed our grant calls to include questions about the liver. There was such hope when the first human clinical trials began for myotubular and centronuclear myopathy, and the difficult years that have ensued since then have shown us how important it continues to be to keep these conditions at the forefront of groundbreaking research.

We are dedicated to continuing to make a meaningful difference - there is clearly a vital role for a disease specific research funder in the world of rare disease, along with a tangible need to support patients and families. We are conscious though of 'Founder syndrome' and the voice of the living patient. We aim to take every opportunity to invite in other patients, parents and families to take key roles and become leading voices in this work. We recognise that no one organisation can provide all the answers, and it is our ambition in the next 5 years to support the initiatives of others, particularly our younger community.

TRUSTEES' ANNUAL REPORT 31 December 2023

Since founding in 2006...we have:

1. Raised over **£2.9M**, through family-led fundraising, networks and relationships.
2. Made **18 research grants** to researchers in world class laboratories, with the support of a highly regarded Scientific Advisory Board.
3. Funded the proof of principle project for gene therapy that led to the **first ever clinical trial** for myotubular myopathy.
4. Funded **other proof of principle projects** that progressed to clinical trial.
5. Funded research grants that contributed to the discovery of **two new genes** implicated in centronuclear and myotubular myopathy.
6. Hosted **five family conferences**, bringing together affected individuals and families, researchers, clinicians, and other health professionals, and arranged several family meetings by **Zoom both during the pandemic and beyond** with presentations from, and discussions with, global experts and scientists.
7. Created the first disease specific international **Patient Registry** to gather vital information on the condition and funded its migration to the stability and credibility of a university setting.
8. Participated in a European Neuromuscular Centre workshop on Mouthpiece Ventilation, resulting in the publication of **MPV international best practice guidelines**.
9. Been invited by **Great Ormond Street Hospital Children's Charity** to be one of their small number of rare disease charity partners in their annual national funding call focusing on complex or rare childhood diseases.
10. Sponsored a **Standards of Care** meeting for clinicians, patients, and their healthcare professionals at the Royal Brompton Hospital.
11. Presented for LifeArc on **drug repurposing for rare diseases** and contributed to their published expert advice.
12. Contributed to the first ever **Congenital Myopathies Masterclass** for European healthcare providers. The Masterclass was organised by TREAT-NMD and included sessions led by world leading experts on myotubular and centronuclear myopathy.
13. Sponsored the UK focus group that contributed to the international study, and subsequent journal publication, **Lessons Learnt from Clinical Studies in Centronuclear Myopathies**.
14. Created a great band of **committed supporters**, raising funds for us year on year.
15. Developed strategic relationships with **key stakeholders** in the fields of neuromuscular disease, rare disease, UK regulatory bodies, and highly regarded UK children's charities including the UK umbrella muscle disease charity, MDUK.
16. And **most importantly**, brought together **families** affected by myotubular and centronuclear myopathy, who support the Trust's fundraising and each other's lives.

In 2023 specifically...we have:

1. Raised £117,500.
2. Continued to substantially add to our Family Factsheets, the purpose of which is to share personal family case studies to support other families in their care and decision making.
3. Invited applications for a joint grant round in partnership with Great Ormond Street Children's Charity.
4. Awarded a £300,000 grant to Dr James Dowling at Sick Kids, Canada to study liver disease in X-linked myotubular myopathy, in partnership with the UK muscle disease charity MDUK.
5. Continued our collaboration with the US patient organisation, MTM-CNM Family Connection, to run the MTM-CNM Liver Collaborative Working Group, bringing together a range of leading global experts, scientists, experienced clinicians, and biotechs, to fast-track cooperation on the understanding of liver issues emerging from current clinical trials.
6. Worked with the Myotubular and Centronuclear Myopathy Patient Registry, through the Liver Collaborative, to develop, launch and promote a new section of academic, clinical

TRUSTEES' ANNUAL REPORT 31 December 2023

- and patient curated questions about liver health, leading to 121 patients sharing their liver data within 4 months.
7. Contributed to an academic presentation based on this data at the World Muscle Society meeting in October 2023.
 8. Co-hosted a webinar for patients and families to hear from worldwide experts on liver issues and recommendations for clinical care.
 9. Set up a research team to investigate possible muscle symptoms and lived experience of xlmtm carrier women in the UK and Ireland and disseminated a survey to carrier women in UK and Ireland which was resoundingly positively received.

Every single year since founding in 2006 we have raised 100% of our running costs separately from the funds raised by families and supporters, meaning that once again in 2023 we met our ambition to channel all the funds raised by supporters into research.

Family Support in 2023

Advocacy and Family Support

Specific support is needed for myotubular and centronuclear myopathy patients and families, mainly because of the rarity of centronuclear and myotubular myopathy. Usually, the child's or patient's GP or doctor will never have come across the condition before - making being diagnosed a frightening and bewildering experience for all concerned. Being hurled suddenly, and usually without warning, into a world of medical jargon; high level nursing; complex healthcare; and social care systems, families and individuals are grateful to know they are not alone, and that we, and others like them, are willing to share the burden of responsibility by helping them understand their experiences and to navigate the systems.

At a time when parents are supposed to be celebrating the birth of an infant, our families are often instead in the position of having to make important choices around giving their child the best quality of life, and a chance of longer-term survival. The information these families are given by their hospital care teams to make those decisions is sometimes inaccurate, often patchy, and even delivered by someone who has never seen a child with the condition before. When a baby is finally stable enough to go home, it is not unusual for the transition process from hospital to home to take 1 year to 18 months.

The need for support/information caused by a lack of understanding of the impacts of such a rare, devastatingly life threatening condition re-emerges many times throughout a patient's life - and again at times of change, such as when there is a physical change (such as losing the ability to walk or developing scoliosis), during periods of ill health, when moving home or into a new phase of education or work, around family planning, or practical day-to-day living issues.

In 2023, while providing individual support for individual issues for families, we also continued to add to **Factsheets**, our substantial repository of publicly available patient case studies and experiences to be shared. We are very grateful to all the patients and families who have contributed to these case studies. They are invaluable.

We also in 2023 continued to advocate for more knowledge to be collated and shared about liver health in myotubular myopathy. As part of the Liver Collaborative Working Group, we advocated for and supported the development of novel guidance on ongoing monitoring, and care for liver health. This **'One Page Liver Information Sheet'** was truly an international initiative and included both muscle and liver contributors from King's College London; Harvard Medical School; Radboud University, The Netherlands; the Hospital for Sick Kids, Toronto; and representatives from the medical teams of the companies who carried out the clinical trials in myotubular and centronuclear myopathy.

TRUSTEES' ANNUAL REPORT 31 December 2023

We also arranged an international education and communication webinar on lessons learnt so far about liver issues and preparing the patient community for the need to gather data on the liver. This webinar was organised in partnership with the US patient advocacy organisation, MTM-CNM Family Connection.

The international study, ***Lessons Learnt from Clinical Studies in Centronuclear Myopathies***, led by Radboud University, the Netherlands, and in which the Myotubular Trust participated, resulted in an academic publication in 2023. The conclusion of the study emphasised the importance of involving patients, caregivers, and patient communities in the design, development, and evaluation of clinical studies and trials. We, and the whole research project team, hope this will provide a valuable resource for those sponsoring clinical trials in the future, and most importantly for patients and their families considering taking part in a clinical trial.

The global closed Facebook group managed by Myotubular Trust – ***Myotubular Myopathy*** - continues to go from strength to strength, with membership reaching 900 members in 2023. This group continues to provide real-time, real-life advice and perspectives for families who regularly tell us they'd be very alone without this community.

Research in 2023

The Myotubular Trust was set up to raise funds to leverage research findings being made, and techniques being trialed, in 'more common' muscle diseases. The ultimate goal of the Trust is to invest in a diverse number of routes to a cure for all genetic forms of myotubular and centronuclear myopathy, or in treatments that alleviate the most severe symptoms. We do this by investing in the very best translational research, peer reviewed to the highest international standards, supported by an eminent Scientific Advisory Board.

Current Grants

Tamoxifen clinical trial

This grant, which is co-funded with Great Ormond Street Hospital Children's Charity, is for the UK arm of a clinical trial to test how the oncology drug, Tamoxifen, works in improving motor and respiratory function in patients with myotubular myopathy. The trial is being led by Dr Giovanni Baranello, and Professor Francesco Muntoni, at the UCL Great Ormond Street Institute of Child Health. In 2023 it completed the recruitment of children in the UK, aged 2 and above, who are affected by x-linked myotubular myopathy, and is part of the global drug repurposing trial that resulted from the work the Myotubular Trust funded with Dr Jim Dowling at Sick Kids Canada. The global trial is led by Dr Dowling and is a double-blind cross over trial - involving 6 months on either a placebo or the drug, with a three month 'wash out period' in between.

Next generation gene therapy

Dr Ana Buj Bello was the recipient of the first ever research grant from the Myotubular Trust in 2008 for her pioneering work on gene replacement therapy for xlmtm. The goal of this latest 2022 grant to Dr Buj Bello and her team at Genethon is to develop an even more specific and potentially safer 'vector' to carry the missing protein, myotubularin, which they hope will ultimately be brought to clinical trial. They also aim to better characterise the liver in laboratory tests, both before and after gene therapy. Based on this understanding and new developments in the technology of AAV vectors, they aim to generate optimised vectors with increased potency and specificity for MTM1 gene delivery.

Studying liver disease in X-linked myotubular myopathy

Dr Jim Dowling has been the recipient of a number of research grants from the Myotubular Trust. The purpose of this 2023 grant to Dr Dowling and his team at Sick Kids is to better understand the cause of liver disease in people living with XLMTM, and to help develop a treatment. It has become clear in recent years that some individuals with X-linked myotubular myopathy can have problems with their liver. Liver complications have also had an impact on

TRUSTEES' ANNUAL REPORT 31 December 2023

the progress of clinical trials. Dr Dowling's work will generate new information on how the liver works in those with XLMTM. This grant was made in partnership with the UK muscle disease charity, MDUK, who are contributing £60,000 over 3 years to the overall grant of £300,000. We are delighted to be partnering with MDUK on this important grant, and believe it is testament to how vital it will be for myotubular myopathy, and likely many other neuromuscular conditions, to better understand the impact of gene therapy, and other treatments, on the liver in clinical trials.

Clinical trial update

Gene therapy

Virus mediated gene therapy received funding from the Myotubular Trust as far back as our first grant award in 2009 to Dr Ana Buj Bello at Genethon, Paris. Dr Buj Bello established proof of principle for this gene therapy, and with the success of her research funded by the Myotubular Trust (grants in 2009 and 2012), other funders subsequently joined in too.

Dosing patients in this trial began in 2018, and it is really important to state that there have been some remarkable outcomes for a number of patients. Ventilator independence has been achieved by boys previously on 24-hour ventilation and generally 'dramatic clinical improvements' were seen, as noted in the academic literature. Essentially, what has been proven is that gene therapy can reverse the severest of symptoms of myotubular myopathy.

Tragically though, 4 young patients died during the trial, and the trial remains on hold while the FDA and the sponsoring company investigate thoroughly. What has become very clear though is that there are aspects of the condition that we do not fully understand yet – including in relation to the liver.

We sincerely thank those affected by myotubular and centronuclear myopathy who took part in this trial and also the antisense trial sponsored by Dynacure that was halted in 2022. As one mother said "It is one thing to live without hope, it is quite another to have hope dashed." Clinical trials, particularly for conditions as severe as ours, require enormous commitment in terms of time, travel, logistics and patience. For the trial to end makes that commitment even harder to endure, and we thank them for that endurance, and for adding to the sum knowledge of our understanding of the condition.

The one clinical trial still ongoing in 2023 was the tamoxifen trial – TAM4MTM. Although the first funding for this trial was in place as early as 2019, setting it up had several setbacks, with Covid having a fundamental impact on timing. The first patients were dosed in Canada in 2021, but it proved more difficult to get it off the ground in the UK and the US. However, the excellent clinical trial team at Great Ormond Street Hospital finally recruited all UK patients in 2023 and began dosing and taking great care of those young boys.

On the road to all these clinical trials, the role of the Trust was to fund the proof of principle/validation work being proposed by so many outstanding researchers, paving the way for companies like Astellas Gene Therapies and Dynacure, or academic institutions such as Sick Kids Toronto and Great Ormond St. London, to take them to clinical trial. That funding makes a fundamental difference, and we are immensely grateful to all our supporters who have made this possible.

We are immensely grateful to our Scientific Advisory Board (SAB) for their time and their expertise and understanding to bring excellence and rigour to our funding decisions. The calibre of applications the Myotubular Trust attracts is due in no small part to the reputation of this group of scientists.

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The academic members of the SAB are:

- Professor Francesco Muntoni, Head of the Dubowitz Neuromuscular Centre, Great Ormond Street Hospital
- Dr Meriel McEntagart, Consultant Clinical Geneticist, St. George's Hospital, London
- Professor Michael Duchen, Professor of Physiology, University College London
- Dr Susan C Brown, previously Reader in Translational Medicine, Department of Veterinary Basic Science, Royal Veterinary College, University of London
- Professor Volker Straub, Harold Macmillan Professor of Medicine, Consultant in Neuromuscular Genetics and Paediatrics, Newcastle University
- Professor Dominic Wells, Professor in Translational Medicine, Royal Veterinary College

We are indebted for the guidance they gave to the Myotubular Trust throughout the year. We are also very grateful to the lay members of our SAB for their time. The lay members include parents, bereaved parents and patients.

Financial Review

Sustainable Fundraising – the Highlights of 2023

The post Covid fundraising landscape has changed substantially, and therefore the Trustees were very grateful that we were able to raise in the region of £120,000 once again this year. Although some challenge-type amateur sporting events have returned since Covid, the sponsorship environment has definitely changed – and people clearly find it harder to ask to be sponsored. This may be due to increasingly constrained personal finances during recent years. Despite that though, our families and their communities continue to find ways to raise funds for us – leveraging the ‘ripple effect’ from each child into an extended network of supporters has been so critical to our growth and stability.

2023 was the year of:

- The 17th Jack Blunsdon Golf Day
- A New Year Sea swim in the cold waters off southern Ireland
- Marathon runners in London, Belfast, Brighton and Dublin
- Half marathon runners in Oldham and Belfast
- Another fantastic Tough Mudder
- Birthday, christening and wedding donations

Sadly, 2023 was another year of many losses and we extend our gratitude to those who, in their time of grief, considered the Myotubular Trust for donations.

A special mention goes once again in 2023 to IGY Foundation who give us so much moral and financial support. Knowing how generous their philanthropy is, we fully realise there are many causes who look to them for help, and we are very grateful that they continue to value the work we do. Their support regularly helps us to be able to meet unexpected needs from research teams, and certainly helps with our running cost pledge.

We also received a very welcome grant of £21,000 from Astellas Pharmaceuticals to provide an educational grant to support the development of a patient leaflet; software development and translation of liver related questions on the patient registry; and educational materials and webinars.

We are also very grateful for the steady income from the supporters from whom we receive standing orders and Give as You Earn schemes during 2023. Thank you to you all.

TRUSTEES' ANNUAL REPORT 31 December 2023

Fundraising Practice

The Trustees take their responsibilities to fundraising very seriously. To that end, we ensure that we adhere to the Fundraising Regulator's code of best practice and meet the Charity Commission's six principles of charity fundraising. For us, at our size, the areas of best practice we pay attention to are;

- providing information on how to fundraise safely,
- considered communication with all fundraisers, which is appropriate to our strategy,
- carrying out a proportionate process of due diligence around fund raising proposals,
- making a record of the issue and return of any charity collection materials,
- securing cash donations and banking them as soon as possible,
- not sharing personal data without explicit consent,
- including opt-out information on fundraising communications sent to a named individual,
- processing unsubscribe requests in a timely way,
- using funds as they have been directed by specific donors, in particular allocating restricted funds appropriately.

We adhere to the Data Protection Act 2018, General Data Protection Regulation (GDPR) and pay data protection fees to the Information Commissioner's Office (ICO).

Reserves Policy

The Trustees sole aim in expending cash reserves is to fund research into a cure or treatment for myotubular myopathy and they do not consider it appropriate to hold long-term reserves.

However, as each research project is granted, those funds will be held available to be released in staged payments, and new awards will only be made if the full cost of the relevant research project is available, and available to be ringfenced. This prudent financial policy is appropriate given our size and specialism.

This policy meant that instead of being hit by a cash flow crisis in 2020 and 2021, and the even worse possibility of not being able to pay for committed research grants, we were even able to announce new grant awards in 2020, announce another grant call for 2021 and prepare to announce another call in 2022 and 2023.

Plans for future periods

The Trust aims in 2024 to:

- Maintain excellence in family support, advocacy, information provision – in particular our Factsheets focus - and continue to make the introductions that families tell us are invaluable.
- Actively promote and support the Liver Questionnaire on the Myotubular and Centronuclear Myopathy Patient Registry to assist in the development of a new academic publication in time for World Muscle Society 2024 – in order to continue the interest in, and commitment to, understanding the liver issue in myotubular myopathy.
- Support the dissemination of liver related resources for patients to share with their medical teams, and liver data to share with the clinical and research communities.
- Promote, and fund, research that furthers our understanding of the liver and bile function in myotubular myopathy, with the goal of being able to impact both clinical trial planning and ongoing patient care.
- Share the results of TAM4MTM, the tamoxifen repurposing trial.

TRUSTEES' ANNUAL REPORT 31 December 2023

- Continue to support the development of a UK carrier women study, building on the excellent work already being done in the Netherlands and Germany.
- Organise webinars on key topics of interest for the patient community and review the appetite for meeting in person once again.
- Continue to work with key stakeholders in the neuromuscular disease community, and strategic rare disease organisations.
- Continue to work with regulatory authorities on behalf of patients with myotubular and centronuclear myopathy.
- Plan ahead and prepare effectively for any future NICE review of treatments for myotubular and centronuclear myopathy, facilitating families' and patients' input.
- Continue to share information with, and promote collaboration between, other family and patient organisations, relevant scientific interest groups and research organisations.
- Continue to secure separate funding to cover the Trust's running costs, while giving our heart felt support all our family-linked fundraisers.

TRUSTEES' ANNUAL REPORT 31 December 2023

Reference and administrative details of the Charity, its Trustees and advisors

The following were Trustees of the Trust and held office during the above period:

Patricia Allen
Gary Browning
Andrew Lennox
Anne Lennox
James Rosling

Trustees are appointed by the board of trustees and serve for three years (five years for Anne Lennox) after which period they may put themselves forward for re-appointment. The trustees meet three times per annum.

Office

Myotubular Trust
- charity registration number 1137177
- company registration number 07260229

15a Barnard Road
London SW11 1QT

Bankers

CAF Bank Limited
Kings Hill
West Mailing
Kent
ME19 4JG

The Co-operative Bank
PO Box 250
Skelmersdale
WN8 6WT

Independent Examiner

Michael Stone MA ACA
Jamieson Stone LLP
Windsor House
40/41 Great Castle Street
London
W1W 8LU

Structure, Governance and Management

Constitution

The Myotubular Trust is an incorporated charity limited by guarantee and its governing document is the memorandum and articles of association dated 21 May 2010. The memorandum and articles of association has the same objects as that of the Trust Deed dated 26 January 2006 of the unincorporated charity. The Trust obtained charitable status under Section 4 of the Charities Act 1960 from the Charity Commission on 19 April 2006 under registration number 1113809 and following incorporation on the 20th May 2010 was registered with the Charity Commission with registration number 1137177, and with Companies House with company registration number 7260229.

Organisation and the Trustees

In selecting individuals for appointment, the trustees will have regard to the skills, knowledge and experience needed for the effective administration of the charity.

TRUSTEES' ANNUAL REPORT 31 December 2023

Trustees' responsibilities statement

The Trustees (who are also directors of The Myotubular Trust for the purposes of company law) are responsible for preparing the Trustees' Report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards.

Company law in England and Wales requires the Trustees to prepare financial statements for each financial year in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards and applicable law). The financial statements are required by law to give a true and fair view of the state of affairs of the charity and of the income and expenditure of the charity for that period. In preparing these financial statements the trustees are required to:

- Select suitable accounting policies and then apply them consistently
- Observe the methods and principles of the Charities SORP
- Make judgments and estimates that are reasonable and prudent
- State whether applicable UK accounting standards have been followed and statements of recommended practice, subject to any departures disclosed and explained in the financial statements and
- Prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue to operate.

The trustees are responsible for keeping accounting records, which disclose with reasonable accuracy at any time the financial position of the charity and enable them to ensure that the financial statements comply with the Companies Act 2006. They are responsible for safeguarding the assets of the charity and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

Risk management

The trustees have examined the strategic, business and operational risks, which the charity faces and confirm that systems have been established to enable regular reports to be produced so that the necessary steps can be taken to lessen the risks.

INDEPENDENT EXAMINER'S REPORT FOR THE YEAR ENDED 31 DECEMBER 2023

Respective responsibilities of trustees and examiner

The trustees (who are also the directors of the company for the purpose of company law) are responsible for the preparation of the accounts. The charity's trustees consider that an audit is not required for this year under section 144 of the Charities Act 2011 (the Charities Act) and that an independent examination is needed.

Having been satisfied that the charity is not subject to audit under company law and is eligible for independent examination it is my responsibility to:

- examine the accounts under section 145 of the Charities Act,
- to follow the procedures laid down in the General Directions given by the Charity Commission (under section 145(5)(b) of the Charities Act, and
- to state whether particular matters have come to my attention.

Basis of independent examiner's statement

My examination was carried out in accordance with the General Directions given by the Charity Commission. An examination includes a review of the accounting records kept by the charity and a comparison of the accounts presented with those records. It also includes consideration of any unusual items or disclosures in the accounts, and the seeking of explanations from you as trustees concerning any such matters. The procedures undertaken do not provide all the evidence that would be required in an audit, and consequently, no opinion is given as to whether the accounts present a 'true and fair view' and the report is limited to those matters set out in the statement below.

Independent examiner's statement

In connection with my examination, no matter has come to my attention:

- 1) which gives me reasonable cause to believe that in, any material respect, the requirements:
 - to keep accounting records in accordance with section 130 of the Charities Act; and
 - to prepare accounts which accord with the accounting records and to comply with the accounting requirements of the Companies Act 2006 and with the methods and principles of the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2019) have not been met; or
- 2) to which, in my opinion, attention should be drawn in order to enable a proper understanding of the accounts to be reached.

Michael Stone

Michael Stone MA ACA
Jamieson Stone LLP
Windsor House
40/41 Great Castle Street
London
W1W 8LU

27 September 2024

STATEMENT OF FINANCIAL ACTIVITIES FOR THE YEAR ENDED 31 DECEMBER 2023

	Unrestricted Funds £	Designated Funds £	Restricted Funds £	Total Funds 2023 £	Total Funds 2022 £
<u>INCOMING RESOURCES</u>					
Donations and grants	42,788	41,000	-	83,788	107,499
Fundraising activities	30,535	-	-	30,535	38,525
Interest received	3,188	-	-	3,188	1,438
	-----	-----	-----	-----	-----
Total incoming resources	76,511	41,000	-	117,511	147,462
	-----	-----	-----	-----	-----
<u>RESOURCES EXPENDED</u>					
Research	-	16,151	-	16,151	40,704
Fundraising costs	(396)	-	-	(396)	-
Outreach work	14	-	-	14	-
Staff costs	49,961	-	-	49,961	49,961
Training	24	-	-	24	-
Accountancy & payroll	236	-	-	236	300
Independent examiner	1,000	-	-	1,000	1,000
Legal & professional	1,262	-	-	1,262	943
Trustee's indemnity	1,009	-	-	1,009	917
Travel costs	120	-	-	120	183
Printing & stationery	25	-	-	25	107
Postage & telephone	122	-	-	122	79
Subscriptions	85	-	-	85	252
Web & IT costs	1,112	-	-	1,112	1,658
Bank charges	109	-	-	109	236
Miscellaneous costs	42	-	-	42	319
	-----	-----	-----	-----	-----
Total resources expended	54,725	16,151	-	70,876	97,944
	-----	-----	-----	-----	-----
Net incoming/(outgoing) resources	21,786	24,849	-	46,635	49,518
Transfers between funds	(10,000)	10,000	-	-	-
	-----	-----	-----	-----	-----
Net movement in funds	11,786	34,849	-	46,635	49,518
	-----	-----	-----	-----	-----
Total funds brought forward	6,323	370,338	-	376,661	327,143
	-----	-----	-----	-----	-----
Total funds carried forward	18,109	405,187	-	423,296	376,661
	-----	-----	-----	-----	-----

All gains and losses arising in the year are included within the statement of financial activities

The accompanying notes form part of these financial statements

BALANCE SHEET AS AT 31 DECEMBER 2023

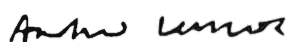
	£	2023 £	£	2022 £
CURRENT ASSETS				
Debtors and prepayments	41,958		32,030	
Cash at bank and in hand	387,268		348,676	
	-----		-----	
Total current assets	429,226		380,706	
	-----		-----	
CREDITORS				
Amounts falling due within one year	5,930		4,045	
	-----		-----	
Net current assets		423,296		376,661
		-----		-----
NET ASSETS		423,296		376,661
		-----		-----
FUNDS OF THE CHARITY				
Restricted funds		-		-
Unrestricted general funds	18,109		6,323	
Unrestricted designated funds	405,187		370,338	
	-----		-----	
		423,296		376,661
		-----		-----

The company is entitled to exemption from audit under Section 477 of the Companies Act 2006 for the year ended 31 December 2023 and the members have not required the company to obtain an audit of its financial statements for the year ended 31 December 2023 in accordance with Section 476 of the Companies Act 2006.

The directors acknowledge their responsibilities for: (a) ensuring that the company keeps accounting records which comply with Sections 386 and 387 of the Companies Act 2006 and (b) preparing financial statements which give a true and fair view of the state of affairs of the company as at the end of each financial year and of its profit or loss for each financial year in accordance with the requirements of Sections 394 and 395 and which otherwise comply with the requirements of the Companies Act 2006 relating to financial statements, so far as applicable to the company.

The financial statements have been prepared in accordance with the provisions of Part 15 of the Companies Act 2006 relating to small companies.

The financial statements were approved by the trustees on 23 September 2024 and signed on their behalf:



.....
Andrew Lennox
Chairman/Trustee



.....
James Rosling
Treasurer/Trustee

The accompanying notes form part of these financial statements

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2023

1. BASIS OF PREPARATION

The financial statements have been prepared on the accruals basis of historic cost in accordance with the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2019) and the Companies Act 2006 and the Charities Act 2011.

2. ACCOUNTING POLICIES

Incoming resources

Incoming resources are recognised when the charity becomes entitled to the resources, the trustees are virtually certain they will receive the resources, and the monetary value can be measured with sufficient reliability.

Where incoming resources have related expenditure (as with fundraising or contract income) the incoming resources and related expenditure are reported gross in the Statement of Financial Activities.

Grants and donations are recognised when the charity has unconditional entitlement to the resources.

Incoming resources from tax reclaims are recognised at the same time as the gift to which they relate.

Contractual income and performance related grants are recognized once the related goods or services have been delivered.

Investment income is included in the accounts when receivable.

Resources expended

Resources expended are recognised as soon as there is legal or constructive obligation committing the charity to pay out resources.

Resources expended include attributable VAT which cannot be recovered.

Funds

Restricted funds are funds to be used for specific purposes as declared by the donor.

Designated funds are monies set aside from general funds and designated for specific research awards by the trustees.

Unrestricted funds are donations and all other incoming resources without a specified purpose and which are available as general funds.

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED)

FOR THE YEAR ENDED 31 DECEMBER 2023

3. TAXATION

The Myotubular Trust is a registered charity and is not liable to Income Tax or Corporation Tax on income derived from its charitable activities.

4. RESOURCES EXPENDED

	2023 £	2022 £
Research	16,151	40,704
Independent examiner's remuneration	1,000	1,000
	-----	-----

The principal research grants awarded during the year were as follows:

	2023 £	2022 £
Hnia at Inserm	9,958	38,929
Inserm(Buj Bello) 2023-25	4,167	-
Newcastle University re Treat NMD	2,026	-
Research Consultancy	-	1,775
	-----	-----

5. DEBTORS AND PREPAYMENTS

	2023 £	2022 £
Gift Aid	458	1,530
Prepayments and accrued income	41,500	30,500
	-----	-----
	41,958	32,030
	-----	-----

6. CREDITORS FALLING DUE WITHIN ONE YEAR

	2023 £	2022 £
Accruals	5,930	4,045
	-----	-----

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED) FOR THE YEAR ENDED 31 DECEMBER 2023

7. RELATED PARTY TRANSACTIONS

There were no related party transactions by the trustees for the year (2022: None).

One Trustee received remuneration of £20,000 during the year ending 31 December 2023 (2022: £20,000).

The trustee's remuneration and other administration costs are funded from unrestricted corporate and charitable donations, which were specifically raised for that purpose.

MYOTUBULAR TRUST

England & Wales - Charity number 1137177

Accounts



Annual Report and Financial Statements

To the year ended
31 December 2022

myotubular trust
FINDING STRENGTH



UK Registered Charity, 1137177
A Company Limited By Guarantee

TRUSTEES' ANNUAL REPORT 31 December 2022

TRUSTEES' ANNUAL REPORT 31 December 2022

The Trustees of the Myotubular Trust take pleasure in presenting their annual report and the financial statements for the year ended 31 December 2022.

Objects and Activities

The objects of the Myotubular Trust as agreed by the Charity Commission are;

- the relief of disability and the extension of life for babies, children and adults suffering from myotubular myopathy
- by promoting the study of, and research into, the treatment and cure of the muscle weakness caused by myotubular myopathy.

The Trust focuses on five outcomes to enable the achievement of these objectives:

1. Bringing families together
2. Promoting and funding international research
3. Sharing knowledge
4. Promoting innovative thinking and collaboration
5. Working with our extended families.

We bring about the public benefit required of all charities, by the activities of:

- making grants to organisations and individuals
- providing support, advice, and information
- sponsoring research.

Myotubular Myopathy and Centronuclear Myopathy

Myotubular myopathy is a rare and extremely life-threatening muscle condition, which causes profound muscle weakness, usually from birth. It is one of a group of conditions called **centronuclear** myopathies – under a microscope the nucleus of the muscle cell of someone affected is in the **centre**, rather than at the edge of the cell.

These conditions are genetic in inheritance. The gene mutation for x-linked myotubular myopathy is carried on the x chromosome (xlmtm), and is the most common form, affecting (mainly) boys. They usually do not survive their babyhood – the statistics have been under review in the last few years and the current view is that 50-75% die in their first year, and very few make it to adulthood. Even rarer genetic forms, either dominant or recessive in inheritance, can affect both males and females and are generally milder in severity. The terms myotubular and centronuclear myopathy both describe 'our' condition.

Children and adults with myotubular myopathy usually require vigilant nursing care, ventilators to breathe, power wheelchairs to get around, and are often fed via a tube into the stomach. Carrier females, and those affected by some of the rarer forms which can manifest in adult life, may develop muscle weakness and problems with eating and drinking; walking and movement; muscle fatigue and susceptibility to respiratory weakness and associated infections.

While myotubular myopathy has historically been considered primarily a muscle disease, and care has focused on these respiratory challenges and complications, the last three years have shone a light on the possible liver complications that some patients may suffer from. In the first two clinical trials for XLMTM and CNM, adverse events were reported in liver function tests, and tragically in particular, there were four deaths related to the liver. A new push in our field will be needed to understand how the liver is impacted and what that means for future clinical trials, and just as importantly for day-to-day care of all patients.

TRUSTEES' ANNUAL REPORT 31 December 2022

2022 – where are we now

In the 17 years since the Myotubular Trust was founded, the landscape has changed markedly. Day to day management of the condition has improved with evolving respiratory support techniques and, wonderfully, many children are living longer. Substantial progress has been made in understanding myotubular and centronuclear myopathy, and research into a treatment, or cure, has made great steps forward, including the first human clinical trials.

However, there remain many questions about the condition, and why and how these genetic mutations, and the proteins they impact, cause muscle weakness. There have been deeply disappointing setbacks in the clinical trials – the gene therapy trial is still on hold after the death of four participating patients; and the ASO trial (explained further below) was terminated due to concerning liver test results. Combined with the history of some (but not all) of those with XLMTM suffering from liver complications over the years, we now urgently need to uncover the true natural history of the liver, and the mechanism of action by which a lack of myotubularin is implicated in the liver.

The Trust was established in 2006 by two parents of boys with myotubular myopathy in order to raise research funds. There was no other way for passionate parents to ring-fence money to fund research into a treatment or cure for this condition, even though we did at the time approach some larger charities for whom we had hoped to fundraise. We also realised very quickly that it was essential to support the profile of the condition within the neuromuscular research community – to compete for brains and innovative ideas – and to support those living with, and bereaved by, myotubular myopathy.

There are new understandings of the condition emerging particularly from the clinical trials, which present several new challenges, but also new avenues of research. We need to be here to voice the urgency of this work, and to be a source of funding too. There was such hope when the first human clinical trials began for myotubular and centronuclear myopathy, and the difficult years that have ensued since then have shown us how important it continues to be to keep these conditions at the forefront of groundbreaking research.

We are dedicated to continuing to make a meaningful difference - there is clearly a vital role for a disease specific research funder in the world of rare disease, along with a tangible need to support patients and families. We are conscious though of 'Founder syndrome' and the voice of the living patient. We aim to take every opportunity to invite in other patients, parents and families to take key roles and become leading voices in this work. We recognise that no one organisation can provide all the answers, and it is our ambition in the next 5 years to support the initiatives of others, particularly our younger community.

TRUSTEES' ANNUAL REPORT 31 December 2022

Since founding in 2006...we have:

1. Raised over **£2.6M**, through family-led fundraising, networks and relationships.
2. Made **17 research grants** to researchers in world class laboratories, with the support of a highly regarded Scientific Advisory Board.
3. Funded the proof of principle project for gene therapy that led to the **first ever clinical trial** for myotubular myopathy.
4. Funded **other proof of principle projects** that progressed to clinical trial.
5. Funded research grants that contributed to the discovery of **two new genes** implicated in centronuclear and myotubular myopathy.
6. Hosted **five (in person) family conferences**, bringing together affected individuals and families, researchers, clinicians, and other health professionals, and arranged several family meetings by **Zoom during the pandemic and beyond** with global experts and scientists.
7. Created the first disease specific international **Patient Registry** to gather vital information on the condition and funded its migration to the stability and credibility of a university setting.
8. Participated in a European Neuromuscular Centre workshop on Mouthpiece Ventilation, resulting in the publication of **MPV international best practice guidelines**.
9. Been invited by **Great Ormond Street Hospital Children's Charity** to be one of their small number of rare disease charity partners in their annual national funding call focusing on complex or rare childhood diseases.
10. Sponsored a **Standards of Care** meeting for clinicians, patients, and their healthcare professionals at the Royal Brompton Hospital.
11. Presented for LifeArc on **drug repurposing for rare diseases** and contributed to their published expert advice.
12. Contributed to the first ever **Congenital Myopathies Masterclass** for European healthcare providers. The Masterclass was organised by TREAT-NMD and included sessions led by world leading experts on myotubular and centronuclear myopathy.
13. Created a great band of **committed supporters**, raising funds for us year on year.
14. Developed strategic relationships with **key stakeholders** in the fields of neuromuscular disease, rare disease, UK regulatory bodies, and highly regarded UK children's charities including the UK umbrella muscle disease charity, MDUK.
15. And **most importantly**, brought together **families** affected by myotubular and centronuclear myopathy, who support the Trust's fundraising and each other's lives.

In 2022 specifically...we have:

1. Raised nearly £150,000.
2. Invited applications for our 13th research grant round, this time in partnership with Muscular Dystrophy UK.
3. Awarded a grant to Dr Ana Buj Bello at Genethon, Paris, to develop an even more specific and potentially safer gene therapy.
4. Promoted, and participated in, a focus group of UK patients and parents as part of *Lessons Learnt from Clinical Studies in Centronuclear Myopathies*, an international study led by Radboud University, the Netherlands, and initiated at the 2022 family conference in Germany, organised by the German patient organisation ZNM-ZusammenStark.
5. Presented at the **MHRA One Agency** annual 'away day', as one of the two charities presenting the patient perspective to the whole staff of the UK drug regulator.
6. Launched, in collaboration with University College Cork, a Home Care survey to gather information on home care packages available in the UK, to support newly diagnosed families with real word evidence.
7. Supported the launch of a 'Burden of Care' survey to the UK myotubular and centronuclear myopathy caregiver community, as part of Astellas Pharmaceutical's gathering of data that will ultimately be used as part of any submission (from any company) to NICE for drug or treatment approval.

TRUSTEES' ANNUAL REPORT 31 December 2022

8. Collaborated with the US patient organisation, MTM-CNM Family Connection, to run the MTM-CNM Liver Collaborative Working Group, bringing together a range of leading global experts, scientists, experienced clinicians, and biotechs to fast-track cooperation on the understanding of liver issues emerging from current clinical trials.
9. Facilitated the development of a Liver Questionnaire, the first new section of the MTM & CNM Patient Registry, again with MTM-CNM Family Connection and the expertise of the Liver Collaborative Working Group.
10. For the 16th year since founding, we have raised 100% of our running costs separately from the funds raised by families and supporters, meaning that once again we meet our ambition to dedicate all the funds raised by supporters into research.

Family Support in 2022

Advocacy and Family Support

In the 17 years from launch in 2006 to 2022 we are regularly reminded that specific support is needed for myotubular and centronuclear myopathy patients and families. This is, in the main, because centronuclear and myotubular myopathy are so rare that usually the child's or patient's GP or doctor will never have come across the condition before - making being diagnosed a frightening and bewildering experience for all concerned. Being hurled suddenly, and usually without warning, into a world of medical jargon, high level nursing, complex healthcare and social care systems, families and individuals are grateful to know they are not alone, and that we, and others like them, are willing to share the burden of responsibility by helping them understand their experiences and to navigate the systems.

At a time when parents are supposed to be celebrating the birth of an infant, our families are often instead in the position of having to make important choices around giving their child the best quality of life, and a chance of longer-term survival. The information these families are given by their hospital care teams to make those decisions is sometimes inaccurate, often patchy, and even delivered by someone who has never seen a child with the condition before. When a baby is finally stable enough to go home, it is not unusual for the transition process from hospital to home to take 1 year to 18 months.

In 2022 we launched a survey, a collaboration between the Myotubular Trust and University College Cork, to gather reliable, objective, analysable data on home care packages in place for myotubular and centronuclear myopathy patients throughout the UK. With that information we hope to be able to support new families and their healthcare teams at a very difficult time.

The need for support/information caused by a lack of understanding of the impacts of such a rare, devastatingly life threatening condition re-emerges many times throughout a patient's life - and more often at times of change, such as when there is a physical change (such as losing the ability to walk or developing scoliosis), during periods of ill health, when moving home or into a new phase of education or work, around family planning, or practical day-to-day living issues. Shared experiences and information signposting are needed again and again by families. In 2022 we continued to add to **Factsheets**, our substantial repository of publicly available patient case studies and experiences to be shared. We are very grateful to all the patients and families who have contributed to these case studies. They are invaluable.

TRUSTEES' ANNUAL REPORT 31 December 2022

Research in 2022

The Myotubular Trust was set up to raise funds to leverage the research findings being made, and techniques being trialed, in 'more common' muscle diseases. The ultimate goal of the Trust is to invest in a diverse number of routes to a cure for all genetic forms of myotubular and centronuclear myopathy, or in treatments that alleviate the most severe symptoms. We do this by investing in the very best translational research, peer reviewed to the highest international standards, supported by an eminent Scientific Advisory Board.

Current Grants

Tamoxifen clinical trial

This grant, which is co-funded with Great Ormond Street Hospital Children's Charity, is for the UK arm of a clinical trial to test how the oncology drug, Tamoxifen, works in improving motor and respiratory function in patients with myotubular myopathy. The trial is being led by Dr Giovanni Baranello, and Professor Francesco Muntoni, at the UCL Great Ormond Street Institute of Child Health. It began recruiting children in the UK, aged 2 and above, who are affected by x-linked myotubular myopathy, and is part of the global drug repurposing trial that resulted from the work the Myotubular Trust funded with Dr Jim Dowling at Sick Kids Canada. The global trial is led by Dr Dowling. The trial is a double-blind cross over trial - involving 6 months on either a placebo or the drug, with a three month 'wash out period' in between.

The mTORC pathway

Dr Karim Hnia at the world-renowned French institute, INSERM, was awarded a 2-year grant in 2020 by Myotubular Trust investigating the question "Is the mTORC1 pathway a route to treatment in x-linked myotubular myopathy?"

mTORC1 is a master regulator of muscle growth – from the early steps of muscle cell differentiation in the womb, to the work of muscles in adult life. The work of Dr Hnia's laboratory has shown that mTORC1 is 'overactivated' when XLMTM is present. What makes this a very interesting project (apart from the highly positive peer review) is that there are a number of drugs already licensed to regulate mTORC1 levels for other diseases.

This grant finished in 2022, having shone new light on how myotubularin controls muscle growth signalling during cell development. This opens up the possibility of identifying drugs that can trigger specific muscle signalling. We anticipate that this work will be published in 2023/34.

Next generation gene therapy

Dr Ana Buj Bello was the recipient of the first ever research grant from the Myotubular Trust for her pioneering work on gene replacement therapy for xlmtm. The goal of this 2022 grant to Dr Buj Bello and her team at Genethon is to develop an even more specific and potentially safer MTM1 vector to be brought to clinical trial. They aim to better characterise the liver in laboratory tests, both before and after gene therapy. Based on this understanding and new developments in the technology of AAV vectors, they will generate optimised vectors with increased potency and specificity for MTM1 gene delivery.

Patient Registry

In order to add the new liver section to the MTM and CNM Patient Registry the Myotubular Trust, together with the MTM-CNM Family Connection in the US, provided a grant to the Newcastle University Registry team to fund the software development and project management of these new questions. It was heartening to see how quickly we could make this happen as a team united behind a very important purpose. The new section will be ready to launch early in 2023.

TRUSTEES' ANNUAL REPORT 31 December 2022

Clinical trial update

Gene therapy

Virus mediated gene therapy received funding from the Myotubular Trust as far back as our first grant award in 2009 to Dr Ana Buj Bello at Genethon, Paris. Dr Buj Bello established proof of principle for this gene therapy, and with the success of her research funded by the Myotubular Trust (grants in 2009 and 2012), other funders subsequently joined in too. *"It is the result of perseverance and joined forces. Thanks a lot for your support all along these years, your contribution has been crucial, you can be proud of it"* Dr Buj Bello

Dosing patients in this trial began in 2018, and there have been some remarkable outcomes for a number of patients. Ventilator independence has been achieved by boys previously on 24-hour ventilation and generally 'dramatic clinical improvements' were seen, as noted in the academic literature. Essentially, what has been proven is that gene therapy can reverse the severest of symptoms of myotubular myopathy.

Tragically though, 4 young patients died during the trial, and it is now on hold while the FDA and the sponsoring company investigate thoroughly. What has become very clear though is that there are aspects of the condition that we do not fully understand yet – including in relation to the liver.

Antisense Therapy

The 3-year grant, *"Reducing DNM2 as a novel therapeutic target for CNM"*, made by the Myotubular Trust to Jocelyn Laporte's team at the laboratory IGBMC in 2016 *"validated a deliverable approach"*, and formed a major contribution to the pre-clinical studies preparing the way for a clinical trial to test this approach in humans who have either the x-linked MTM or Dynamin 2 form of the condition.

In 2019, Dynacure, a start-up biotech based in Strasbourg, secured approval for a clinical trial for those affected by the MTM1 and DNM2 genes, and this trial was due to begin in 2020. One patient began treatment, but unfortunately the pandemic put the trial on pause for a number of months. However, by the end of 2020 recruitment was restored, and initial dosing began in several countries in Europe, including in the UK. This progressed throughout 2021, but to all our shared disappointment, the trial was halted in the autumn of 2022 due to the reporting of adverse events, specifically elevated liver test results and low blood platelet counts. These were ultimately resolved for each patient by stopping treatment, but the company decided that they could no longer pursue this work without understanding why the liver seems to be affected in this condition.

'This is not the news we ever wanted to share, as we know how great your needs are for safe and effective treatments. As a company, and as individuals, we are overwhelmed with disappointment' Chris Freitag, Chief Medical Officer, Dynacure.

One of our major learnings through this heart-breaking process was the value of our rare disease data. It is not unusual when a clinical trial is halted, for all the data to be abandoned. However, the researchers involved both from the company, and the Principal Investigators from specific trial sites, were committed to saving, using and publishing as much data as possible. In the months after the trial stoppage was announced, and before the company formally terminated the project, they worked together to develop ways to save and store the data, and routes to publication. We know now that this is not usual, and we are very grateful to those individuals involved.

We also sincerely thank those affected by myotubular and centronuclear myopathy who took part in this trial. As one mother said "It is one thing to live without hope, it is quite another to have hope dashed." Clinical trials, particularly for conditions as severe as ours, require

TRUSTEES' ANNUAL REPORT 31 December 2022

enormous commitment in terms of time, travel, logistics and patience. For the trial to end makes that commitment even harder to endure, and we thank them for that endurance, for adding to the sum knowledge of our understanding of the condition.

Tamoxifen clinical trial

Setting up this trial has had a number of setbacks, with Covid having a not insubstantial impact on timing. The first patients were dosed in Canada in 2021, but it proved more difficult to get it off the ground in the UK and the US. However, 2022 was a year where as team – researchers, clinicians and patients - we worked hard to push to solve a number of blockages, and as the year ended everything was ready for the trial to begin recruitment in the UK early in 2023.

On the road to all these clinical trials, the role of the Trust was to fund the proof of principle/validation work being proposed by these outstanding researchers, paving the way for companies like Astellas Gene Therapies and Dynacure, or academic institutions such as Sick Kids Toronto and Great Ormond St. London, to take them to clinical trial. That funding makes a fundamental difference, and we are immensely grateful to all our supporters who have made this possible.

We are immensely grateful to our Scientific Advisory Board (SAB) for their time and their expertise and understanding. The calibre of applications the Myotubular Trust attracts is due in no small part to the reputation of this group of scientists.

The academic members of the SAB are:

- Professor Francesco Muntoni, Head of the Dubowitz Neuromuscular Centre, Great Ormond Street Hospital
- Dr Meriel McEntagart, Consultant Clinical Geneticist, St. George's Hospital, London
- Professor Michael Duchen, Professor of Physiology, University College London
- Dr Susan C Brown, previously Reader in Translational Medicine, Department of Veterinary Basic Science, Royal Veterinary College, University of London
- Professor Volker Straub, Harold Macmillan Professor of Medicine, Consultant in Neuromuscular Genetics and Paediatrics, Newcastle University
- Professor Dominic Wells, Professor in Translational Medicine, Royal Veterinary College

We are indebted for the guidance they gave to the Myotubular Trust throughout the year. We are also very grateful to the lay members of our SAB for their time. The lay members include parents, bereaved parents and patients.

TRUSTEES' ANNUAL REPORT 31 December 2022

Financial Review

Sustainable Fundraising – the Highlights of 2022

There is no doubt that the post Covid fundraising landscape has changed fundamentally, and therefore the Trustees were very grateful that we were able to raise in the region of £150,000 once again this year - £146,024 to be precise. Although challenge-type amateur sporting events have come back to some degree since Covid, willingness to look for sponsorship seems to have reduced, based on our experience over the last 16 years. This may be due to increasingly constrained personal finances during recent years. Despite that though, our families and their communities continue to find ways to raise funds for us – leveraging the 'ripple effect' from each child into an extended network of supporters has been so critical to our growth and stability.

2022 was the year of:

- The 16th Jack Blunsdon Golf Day
- A 100km walk from Team Robin
- A New Year sea swim in the cold waters off Ireland!
- The Six Peaks Challenge team
- Summer festival in Germany and evening event in Northern Ireland
- A brave London Marathon runner
- The Manchester intrepid Half Marathon runner
- Birthday donations
- Everest Trek by Team Noah
- A School dress down day
- Christmas donations in lieu of cards

We also were delighted to receive an Amazon Community UK donation following a nomination by a member of Team Robin.

Sadly, 2022 was another year of many losses and we extend our gratitude to the families and friends of those boys who, in their time of grief, considered the Myotubular Trust for donations.

We were fortunate that the generous post-Covid funding from the Global's Make Some Noise appeal continued through 2022 and we cannot thank them enough for their interest in our small charity, and the care they took of us. Speaking of financial and moral support, a special mention goes once again to IGY Foundation who are so good to us, when we fully realise there are many causes who must look to them for help. Thank you for seeing the value of the work we do.

Once again we had an increase in standing orders during 2022, probably as people realised how difficult it was for charities during social distancing and lockdowns. Thank you to you all.

Fundraising Practice

The Trustees take their responsibilities to fundraising very seriously. To that end, we ensure that we adhere to the Fundraising Regulator's code of best practice and meet the Charity Commission's six principles of charity fundraising. For us, at our size, the areas of best practice we pay attention to are;

- providing information on how to fundraise safely,
- considered communication with all fundraisers, which is appropriate to our strategy,
- carrying out a proportionate process of due diligence around fund raising proposals,
- making a record of the issue and return of any charity collection materials,
- securing cash donations and banking them as soon as possible,
- not sharing personal data without explicit consent,
- including opt-out information on fundraising communications sent to a named individual,
- processing unsubscribe requests in a timely way,
- using funds as they have been directed by specific donors, in particular allocating restricted funds appropriately.

TRUSTEES' ANNUAL REPORT 31 December 2022

We adhere to the Data Protection Act 2018, General Data Protection Regulation (GDPR) and pay data protection fees to the Information Commissioner's Office (ICO).

Reserves Policy

The Trustees sole aim in expending cash reserves is to fund research into a cure or treatment for myotubular myopathy and they do not consider it appropriate to hold long-term reserves.

However, as each research project is granted, those funds will be held available to be released in staged payments, and new awards will only be made if the full cost of the relevant research project is available, and available to be ringfenced. This prudent financial policy is appropriate given our size and specialism.

This policy meant that instead of being hit by a cash flow crisis in 2020 and 2021, and the even worse possibility of not being able to pay for committed research grants, we were even able to announce new grant awards in 2020, announce another grant call for 2021 and prepare to announce another call in 2022.

Plans for future periods

The Trust aims in 2023 to:

- Maintain excellence in family support, advocacy, information provision, and continue to make the introductions that families tell us are invaluable.
- Finalise the development, and actively promote and support the launch, of the Liver Questionnaire on the Myotubular and Centronuclear Myopathy Patient Registry.
- Organise an international education and communication webinar on lessons learnt so far about liver issues and preparing the patient community for the need to gather data on the liver.
- Facilliate and support the development of liver related resources for patients to share with their medical teams, and liver data to share with the clinical and research communities.
- Award a grant (or grants) to further the understanding of the liver and bile function in myotubular myopathy, with the goal of being able to impact both clinical trial planning and ongoing patient care.
- Share the results of TAM4MTM, the tamoxifen repurposing trial.
- Share the publication of the work of Dr Karim Hnia on mTORC signalling in mtm.
- Continue to work with key stakeholders in the neuromuscular disease community, and strategic rare disease organisations.
- Continue to work with regulatory authorities on behalf of patients with myotubular and centronuclear myopathy.
- Plan ahead and prepare effectively for any future NICE review of treatments for myotubular and centronuclear myopathy, facilitating families' and patients' input.
- Continue to share information with, and promote collaboration between, other family and patient organisations, relevant scientific interest groups and research organisations.
- Continue to secure separate funding to cover the Trust's running costs.

TRUSTEES' ANNUAL REPORT 31 December 2022

Reference and administrative details of the Charity, its Trustees and advisors

The following were Trustees of the Trust and held office during the above period:

Patricia Allen

Gary Browning

Greg Fowler (resigned 22 September 2022)

Andrew Lennox

Anne Lennox

James Rosling

Trustees are appointed by the board of trustees and serve for three years (five years for Anne Lennox) after which period they may put themselves forward for re-appointment. The trustees meet three times per annum.

Office

Myotubular Trust

- charity registration number 1137177

- company registration number 07260229

15a Barnard Road
London SW11 1QT

Bankers

CAF Bank Limited

Kings Hill

West Mailing

Kent

ME19 4JG

The Co-operative Bank

PO Box 250

Skelmersdale

WN8 6WT

Independent Examiner

Michael Stone MA ACA

Jamieson Stone LLP

Windsor House

40/41 Great Castle Street

London

W1W 8LU

Structure, Governance and Management

Constitution

The Myotubular Trust is an incorporated charity limited by guarantee and its governing document is the memorandum and articles of association dated 21 May 2010. The memorandum and articles of association has the same objects as that of the Trust Deed dated 26 January 2006 of the unincorporated charity. The Trust obtained charitable status under Section 4 of the Charities Act 1960 from the Charity Commission on 19 April 2006 under registration number 1113809 and following incorporation on the 20th May 2010 was registered with the Charity Commission with registration number 1137177, and with Companies House with company registration number 7260229.

Organisation and the Trustees

In selecting individuals for appointment, the trustees will have regard to the skills, knowledge and experience needed for the effective administration of the charity.

TRUSTEES' ANNUAL REPORT 31 December 2022

Trustees' responsibilities statement

The Trustees (who are also directors of The Myotubular Trust for the purposes of company law) are responsible for preparing the Trustees' Report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards.

Company law in England and Wales requires the Trustees to prepare financial statements for each financial year in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards and applicable law). The financial statements are required by law to give a true and fair view of the state of affairs of the charity and of the income and expenditure of the charity for that period. In preparing these financial statements the trustees are required to:

- Select suitable accounting policies and then apply them consistently
- Observe the methods and principles of the Charities SORP
- Make judgments and estimates that are reasonable and prudent
- State whether applicable UK accounting standards have been followed and statements of recommended practice, subject to any departures disclosed and explained in the financial statements and
- Prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue to operate.

The trustees are responsible for keeping accounting records, which disclose with reasonable accuracy at any time the financial position of the charity and enable them to ensure that the financial statements comply with the Companies Act 2006. They are responsible for safeguarding the assets of the charity and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

Risk management

The trustees have examined the strategic, business and operational risks, which the charity faces and confirm that systems have been established to enable regular reports to be produced so that the necessary steps can be taken to lessen the risks.

INDEPENDENT EXAMINER'S REPORT FOR THE YEAR ENDED 31 DECEMBER 2022

Respective responsibilities of trustees and examiner

The trustees (who are also the directors of the company for the purpose of company law) are responsible for the preparation of the accounts. The charity's trustees consider that an audit is not required for this year under section 144 of the Charities Act 2011 (the Charities Act) and that an independent examination is needed.

Having been satisfied that the charity is not subject to audit under company law and is eligible for independent examination it is my responsibility to:

- examine the accounts under section 145 of the Charities Act,
- to follow the procedures laid down in the General Directions given by the Charity Commission (under section 145(5)(b) of the Charities Act, and
- to state whether particular matters have come to my attention.

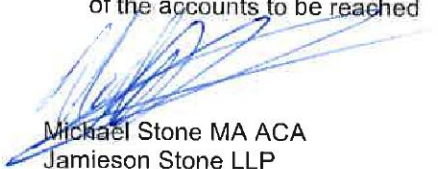
Basis of independent examiner's statement

My examination was carried out in accordance with the General Directions given by the Charity Commission. An examination includes a review of the accounting records kept by the charity and a comparison of the accounts presented with those records. It also includes consideration of any unusual items or disclosures in the accounts, and the seeking of explanations from you as trustees concerning any such matters. The procedures undertaken do not provide all the evidence that would be required in an audit, and consequently, no opinion is given as to whether the accounts present a 'true and fair view' and the report is limited to those matters set out in the statement below.

Independent examiner's statement

In connection with my examination, no matter has come to my attention:

- 1) which gives me reasonable cause to believe that in, any material respect, the requirements:
 - to keep accounting records in accordance with section 130 of the Charities Act; and
 - to prepare accounts which accord with the accounting records and to comply with the accounting requirements of the Companies Act 2006 and with the methods and principles of the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2015) have not been met; or
- 2) to which, in my opinion, attention should be drawn in order to enable a proper understanding of the accounts to be reached



Michael Stone MA ACA
Jamieson Stone LLP
Windsor House
40/41 Great Castle Street
London
W1W 8LU

25/9/2022

STATEMENT OF FINANCIAL ACTIVITIES FOR THE YEAR ENDED 31 DECEMBER 2022

	Unrestricted Funds £	Designated Funds £	Restricted Funds £	Total Funds 2022 £	Total Funds 2021 £
<u>INCOMING RESOURCES</u>					
Donations and grants	43,159	64,340	-	107,499	101,003
Fundraising activities	38,525	-	-	38,525	43,028
Interest received	1,438	-	-	1,438	739
Total incoming resources	83,122	64,340	-	147,462	144,770
<u>RESOURCES EXPENDED</u>					
Research	-	40,704	-	40,704	41,289
Fundraising costs	1,285	-	-	1,285	464
Outreach work	-	-	-	-	2,500
Staff costs	49,961	-	-	49,961	49,961
Training	-	-	-	-	719
Advocacy	-	-	-	-	13,000
Family Conference costs	-	-	-	-	150
Accountancy & payroll	300	-	-	300	140
Independent examiner	1,000	-	-	1,000	1,000
Legal & professional	943	-	-	943	445
Trustee's indemnity	917	-	-	917	873
Travel costs	183	-	-	183	-
Printing & stationery	107	-	-	107	89
Postage & telephone	79	-	-	79	11
Subscriptions	252	-	-	252	174
Web & IT costs	1,658	-	-	1,658	1,497
Bank charges	236	-	-	236	214
Miscellaneous costs	319	-	-	319	104
Total resources expended	57,240	40,704	-	97,944	112,630
Net incoming/(outgoing) resources	25,882	23,636	-	49,518	32,140
Transfers between funds	(26,260)	26,260	-	-	-
Net movement in funds	(378)	49,896	-	49,518	32,140
Total funds brought forward	6,701	320,442	-	327,143	295,003
Total funds carried forward	6,323	370,338	-	376,661	327,143

All gains and losses arising in the year are included within the statement of financial activities

The accompanying notes form part of these financial statements

BALANCE SHEET AS AT 31 DECEMBER 2022

	£	2022 £	£	2021 £
CURRENT ASSETS				
Debtors and prepayments	32,030		25,419	
Cash at bank and in hand	348,676		303,447	
Total current assets	380,706		328,866	
CREDITORS				
Amounts falling due within one year	4,045		1,723	
Net current assets		376,661		327,143
NET ASSETS		376,661		327,143
FUNDS OF THE CHARITY				
Restricted funds		-		-
Unrestricted general funds		6,323		6,701
Unrestricted designated funds		370,338		320,442
		376,661		327,143

The company is entitled to exemption from audit under Section 477 of the Companies Act 2006 for the year ended 31 December 2022 and the members have not required the company to obtain an audit of its financial statements for the year ended 31 December 2022 in accordance with Section 476 of the Companies Act 2006.

The directors acknowledge their responsibilities for: (a) ensuring that the company keeps accounting records which comply with Sections 386 and 387 of the Companies Act 2006 and (b) preparing financial statements which give a true and fair view of the state of affairs of the company as at the end of each financial year and of its profit or loss for each financial year in accordance with the requirements of Sections 394 and 395 and which otherwise comply with the requirements of the Companies Act 2006 relating to financial statements, so far as applicable to the company.

The financial statements have been prepared in accordance with the provisions of Part 15 of the Companies Act 2006 relating to small companies.

The financial statements were approved by the trustees on 25/9/2023 and signed on their behalf:



Andrew Lennox
Chairman/Trustee



James Rosling
Treasurer/Trustee

The accompanying notes form part of these financial statements

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2022

1. BASIS OF PREPARATION

The financial statements have been prepared on the accruals basis of historic cost in accordance with the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2015) and the Companies Act 2006 and the Charities Act 2011.

2. ACCOUNTING POLICIES

Incoming resources

Incoming resources are recognised when the charity becomes entitled to the resources, the trustees are virtually certain they will receive the resources, and the monetary value can be measured with sufficient reliability.

Where incoming resources have related expenditure (as with fundraising or contract income) the incoming resources and related expenditure are reported gross in the Statement of Financial Activities.

Grants and donations are recognised when the charity has unconditional entitlement to the resources.

Incoming resources from tax reclaims are recognised at the same time as the gift to which they relate.

Contractual income and performance related grants are recognized once the related goods or services have been delivered.

Investment income is included in the accounts when receivable.

Resources expended

Resources expended are recognised as soon as there is legal or constructive obligation committing the charity to pay out resources.

Resources expended include attributable VAT which cannot be recovered.

Funds

Restricted funds are funds to be used for specific purposes as declared by the donor.

Designated funds are monies set aside from general funds and designated for specific research awards by the trustees.

Unrestricted funds are donations and all other incoming resources without a specified purpose and which are available as general funds.

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED) FOR THE YEAR ENDED 31 DECEMBER 2022

3. TAXATION

The Myotubular Trust is a registered charity and is not liable to Income Tax or Corporation Tax on income derived from its charitable activities.

4. RESOURCES EXPENDED

	2022 £	2021 £
Research	40,704	41,289
Independent examiner's remuneration	1,000	1,000
	<u>41,704</u>	<u>42,289</u>

The principal research grants awarded during the year were as follows:

	2022 £	2021 £
Hnia at Inserm	38,929	29,059
Tamoxifen Protocol	-	2,469
Newcastle University re Treat NMD	-	7,500
Research Consultancy	1,775	2,261
	<u>40,704</u>	<u>39,289</u>

5. DEBTORS AND PREPAYMENTS

	2022 £	2021 £
Gift Aid	1,530	419
Prepayments and accrued income	30,500	25,000
	<u>32,030</u>	<u>25,419</u>

6. CREDITORS FALLING DUE WITHIN ONE YEAR

	2022 £	2021 £
Accruals	4,045	1,723
	<u>4,045</u>	<u>1,723</u>

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED) FOR THE YEAR ENDED 31 DECEMBER 2022

7. RELATED PARTY TRANSACTIONS

There were no related party transactions by the trustees for the year (2021: None).

One Trustee received remuneration of £20,000 during the year ending 31 December 2022 (2021: £20,000).

The trustee's remuneration and other administration costs are funded from unrestricted corporate and charitable donations, which were specifically raised for that purpose.

MYOTUBULAR TRUST

England & Wales - Charity number 1137177

Accounts



Annual Report and Financial Statements

To the year ended
31 December 2021

myotubular trust
FINDING STRENGTH



UK Registered Charity, 1137177
A Company Limited By Guarantee

TRUSTEES' ANNUAL REPORT 31 December 2021

TRUSTEES' ANNUAL REPORT 31 December 2021

The Trustees of the Myotubular Trust take pleasure in presenting their annual report and the financial statements for the year ended 31 December 2021.

Objects and Activities

The objects of the Myotubular Trust as agreed by the Charity Commission are;

- the relief of disability and the extension of life for babies, children and adults suffering from myotubular myopathy,
- by promoting the study of, and research into, the treatment and cure of the muscle weakness caused by myotubular myopathy.

The Trust focuses on five outcomes to enable the achievement of these objectives:

1. Bringing families together
2. Promoting and funding international research
3. Sharing knowledge
4. Promoting innovative thinking and collaboration
5. Working with our extended families.

We bring about the public benefit required of all charities, by the activities of:

- making grants to organisations and individuals.
- providing support, advice, and information.
- sponsoring research.

Myotubular Myopathy and Centronuclear Myopathy

Myotubular myopathy is a rare and extremely life-threatening muscle condition, which causes profound muscle weakness, usually from birth. It is one of a group of conditions called centronuclear myopathies – called this because under a microscope the nucleus of the muscle cell of someone affected is in the centre, rather than at the edge of the cell.

These conditions are genetic in inheritance. The gene mutation for x-linked myotubular myopathy is carried on the x chromosome (xlmtm), and is the most common form, affecting (mainly) boys. They usually do not survive their babyhood – the statistics have been under review in the last few years and the current view is that 50-75% die in their first year, and very few make it to adulthood.

Even rarer genetic forms, either dominant or recessive in inheritance, can affect both males and females and are generally milder in severity. The terms myotubular and centronuclear myopathy both describe 'our' condition.

Children and adults with myotubular myopathy usually require vigilant nursing care, ventilators to breathe, power wheelchairs to get around, and are often fed via a tube into the stomach. Carrier females, and those affected by some of the rarer forms which can manifest in adult life, may develop muscle weakness and problems with eating and drinking; walking and movement; muscle fatigue and susceptibility to respiratory weakness and associated infections.

In 2021, a young boy who was taking part in the gene therapy trial for x-linked myotubular myopathy sadly died. We would like to take this opportunity to extend the deepest sympathies of the Myotubular Trust to his family and those who loved and took care of him. This was the fourth death in the gene therapy trial. As a result the trial has been put on hold by the FDA.

TRUSTEES' ANNUAL REPORT 31 December 2021

Taking stock in 2021

February 2021 marked 15 years since the founding of the Myotubular Trust. The year 2021 also marked 25 years since the laboratory of Jocelyn Laporte in Strasbourg discovered the *mtm1* gene. In the 25 years since then, and the 15 years since the Trust was founded, substantial progress has been made in understanding myotubular and centronuclear myopathy. Research into a treatment, or cure, has made great steps forward; the first clinical trials in humans have begun; and there have been life enhancing and life lengthening improvements in supportive care for those living with myotubular and centronuclear myopathy.

However there remain many questions about the condition, and why and how these genetic mutations, and the proteins they impact, cause muscle weakness. There have been deeply disappointing setbacks in the clinical trials, particularly the gene therapy trial, which is now on hold after the death of 4 participating patients. Young boys also continue to die from the complications caused by myotubular myopathy, and for our community 2021 was a particularly tragic year of losses, leaving behind many heartbroken families.

The Trust was established in 2006 by two parents of boys with myotubular myopathy in order to raise research funds. There was no other way for passionate parents to ring-fence money to fund research into a treatment or cure for this condition, even though we did at the time approach some larger charities for whom we had hoped to fundraise. We also realised very quickly that it was essential to support the profile of the condition within the neuromuscular research community – to compete for brains and innovative ideas – and to support those living with, and bereaved by, myotubular myopathy.

In 2021, after a decade and a half, we took stock of where the Myotubular Trust was at, and although we take great comfort in knowing that we, with the support of so many families, have made a real and substantial difference to progress in finding a cure or treatment for this condition, it is very clear that there remains a lot more to be done. There are new understandings of the condition particularly emerging from the clinical trials, which present a number of new challenges, but also new avenues of research. We need to be here to voice the urgency of this work, and to be a source of funding too. We know that after these two incredibly difficult years it is now more important than ever to keep myotubular myopathy at the forefront of groundbreaking research.

We are dedicated to continuing to make a meaningful difference - there is clearly a vital role for a disease specific research funder in the world of rare disease, along with a tangible need to support patients and families. We are conscious though of 'Founder syndrome' and the voice of the living patient. We aim to take every opportunity to invite in other patients, parents and families to take key roles and become leading voices in this work. We recognise that no one organisation can provide all the answers, and it is our ambition in the next 5 years to support the initiatives of others, particularly our younger community.

TRUSTEES' ANNUAL REPORT 31 December 2021

Since founding in 2006...we have:

1. Raised over **£2.5M**, through family-led fundraising, networks and relationships.
2. Made **16 research grants** to researchers in world class laboratories, with the support of a highly regarded Scientific Advisory Board.
3. Funded the proof of principle project for gene therapy that led to the **first ever clinical trial** for myotubular myopathy.
4. Funded **other proof of principle projects** that are in clinical trial.
5. Funded research grants that contributed to the discovery of **two new genes** implicated in centronuclear and myotubular myopathy.
6. Hosted **five (in person) family conferences**, bringing together affected individuals and families, researchers, clinicians, and other health professionals, and arranged a number of family meetings by **Zoom during the pandemic with global experts and scientists**.
7. Created the first disease specific international **Patient Registry** to gather vital information on the condition and funded its migration to the stability and credibility of a university setting.
8. Sponsored a **Standards of Care** meeting for clinicians, patients, and their healthcare professionals at the Royal Brompton Hospital.
9. Participated in a European Neuromuscular Centre workshop on Mouthpiece Ventilation, resulting in the publication of **MPV international best practice guidelines**.
10. Created a great band of **committed supporters**, raising funds for us year on year.
11. Developed strategic relationships with **key stakeholders** in the fields of neuromuscular disease, rare disease, UK regulatory bodies, and highly regarded UK children's charities.
12. And *most importantly*, brought together **families** affected by myotubular and centronuclear myopathy, who support the Trust's fundraising and each other's lives.

In 2021 specifically...we have:

1. Raised nearly £150,000.
2. Invited applications for our 12th research grant round.
3. Organised and hosted a Scientific Update webinar for patients and families, with leading experts presenting on clinical trial updates, liver issues, drug repurposing and Covid-19.
4. Organised and hosted a webinar for the UK patient community on 'Coping through Covid and beyond', delivered by a counselling psychologist from the Royal Brompton Hospital, London.
5. Presented at the symposium 'Turning the Tide – respiratory management of neuromuscular patients in the era of new treatments'.
6. Partnered with the UK regulator, the MHRA, to do a joint presentation on '*Patients as Partners in Medicines Development*' at the BioIndustry Association – MHRA Regulatory Innovation Conference.
7. Presented for LifeArc on drug repurposing for rare diseases and contributed to their published expert advice.
8. Developed, in collaboration with University College Cork, a HomeCare survey to gather information on home care packages.
9. Collaborated with the US patient organisation, MTM-CNM Family Connection, to set up a condition specific Liver Discussion Workgroup, bringing together a range of leading experts, experienced clinicians, and biotechs to fast-track cooperation on the understanding of liver issues emerging from current clinical trials.
10. Contributed to the first ever Congenital Myopathies Masterclass for European healthcare providers. The Masterclass was organised by TREAT-NMD and included sessions led by world leading experts on myotubular and centronuclear myopathy.
11. For the 15th year since founding, we have raised 100% of our running costs separately from the funds raised by families and supporters, meaning that once again we meet our ambition to dedicate all the funds raised by supporters into research.

TRUSTEES' ANNUAL REPORT 31 December 2021

Family Support in 2021

Advocacy and Family Support

We continued, in 2021, to provide by phone and conference call facility, the support we provided in person pre-pandemic. We also ensured that the most up to date information on Covid 19 and vaccinations for those living with NMD was available for families, and we collaborated with the UK muscle disease charity, MDUK, to channel specific questions from patients directly to relevant experts.

We learnt very early on in the Trust's 15 years that specific support is needed for myotubular and centronuclear myopathy patients and families. This is, in the main, because centronuclear and myotubular myopathy are so rare that usually the child's or patient's GP or doctor will never have come across the condition before - making being diagnosed a frightening and bewildering experience for all concerned. Being hurled suddenly, and usually without warning, into a world of medical jargon, high level nursing, complex healthcare and social care systems, families and individuals are grateful to know they are not alone, and that we, and others like them, are willing to share the burden of responsibility by helping them understand their experiences and to navigate the systems.

At a time when parents are supposed to be celebrating the birth of an infant, our families are often instead in the position of having to make important choices around giving their child the best quality of life, and a chance of longer-term survival. The information these families are given to make those decisions is sometimes inaccurate, often patchy, and even delivered by someone who has never seen a child with the condition before.

When a baby is finally stable enough to go home, it is not unusual for the transition process from hospital to home to take 1 year to 18 months. There are huge differences between the capability of different hospitals, different clinical commissioning groups, and different community nursing support services in making this happen in a timely fashion. This has been further complicated since the pandemic began given the challenges of bringing together the multi-disciplinary teams necessary for this complex step, and the high demand for respiratory and ventilatory trained agency staff.

Therefore, in 2021, we developed a survey, in collaboration with University College Cork, to gather reliable, objective, analysable data on home care packages in place for myotubular and centronuclear myopathy patients throughout the UK. With that information we hope to be able to support new families and their healthcare teams at a very difficult time.

The need caused by a lack of understanding of the impacts of such a rare, devastatingly life threatening condition re-emerges many times throughout a patient's life - and more often at times of change, such as when there is a physical change (such as losing the ability to walk or scoliosis), during periods of ill health, when moving home or into a new phase of education or work, around family planning, or practical day-to-day living issues. So often experiences and information signposting are needed again and again by families. In 2021 we have built up a substantial repository of publicly available patient case studies and experiences to be shared. We are very grateful to all the patients and families who have contributed to these case studies. They are invaluable.

TRUSTEES' ANNUAL REPORT 31 December 2021

Research in 2021

The Myotubular Trust was set up to raise funds to leverage the research findings being made, and techniques being trialled, in 'more common' muscle diseases. The ultimate goal of the Trust is to invest in a diverse number of routes to a cure for all genetic forms of myotubular and centronuclear myopathy, or in treatments that alleviate the most severe symptoms. This we do by investing in the very best translational research, peer reviewed to the highest international standards, supported by an eminent Scientific Advisory Board.

Grants in progress

Tamoxifen clinical trial

This grant, which is co-funded with Great Ormond Street Hospital Children's Charity, is for the UK arm of a clinical trial to test how well the well-known oncology drug, Tamoxifen, works in improving motor and respiratory function in patients with myotubular myopathy. The trial is being led by Dr Giovanni Baranello, and Professor Francesco Muntoni, at the UCL Great Ormond Street Institute of Child Health. It will involve children in the UK who are affected by x-linked myotubular myopathy, and is part of the global drug repurposing trial that resulted from the work the Trust funded with Dr Jim Dowling at Sick Kids Canada. The global trial is led by Dr Dowling.

The mTORC pathway

Dr Karim Hnia at the world-renowned French institute, INSERM, with 2-year Myotubular Trust funding is investigating the question "Is the mTORC1 pathway a route to treatment in x-linked myotubular myopathy?"

mTORC1 is a master regulator of muscle growth – from the early steps of muscle cell differentiation in the womb, to the work of muscles in adult life. The work of Dr Hnia's laboratory has shown that mTORC1 is 'overactivated' when XLMTM is present. What makes this a very interesting project (apart from the highly positive peer review) is that there are a number of drugs already licensed to regulate mTORC1 levels for other diseases.

Clinical trial update

Gene therapy

Virus mediated gene therapy received funding from the Myotubular Trust as far back as our first grant award in 2009 to Dr Ana Buj Bello at Genethon, Paris. Dr Buj Bello established proof of principle for this gene therapy, and with the success of her research funded by the Trust (grants in 2009 and 2012), other funders subsequently joined in too. *"It is the result of perseverance and joined forces. Thanks a lot for your support all along these years, your contribution has been crucial, you can be proud of it"* Dr Buj Bello

Dosing patients in this trial began in 2018, and there have been some remarkable outcomes for a number of patients. Ventilator independence has been achieved by boys previously on 24 hour ventilation and generally 'dramatic clinical improvements' were seen, as noted in the academic literature. Essentially, what has been proven is that gene therapy can reverse the severest of symptoms of myotubular myopathy.

Tragically though, 4 young patients died during the trial and it is now on hold while the FDA and the sponsoring company investigate thoroughly. What has become very clear though is that there are aspects of the condition that we do not fully understand yet – including in relation to the liver.

TRUSTEES' ANNUAL REPORT 31 December 2021

Antisense Therapy

The 3 year grant, “*Reducing DNM2 as a novel therapeutic target for CNM*”, made by the Myotubular Trust to Jocelyn Laporte’s team at the laboratory IGBMC in 2016 “*validated a deliverable approach*”, and formed a major contribution to the pre-clinical studies preparing the way for a clinical trial to test this approach in humans—who have either the x-linked MTM or Dynamin 2 form of the condition.

In 2019, Dynacure, a start-up biotech based in Strasbourg, secured approval for a clinical trial for those affected by the MTM1 and DNM2 genes, and this trial was due to begin in 2020. One patient began treatment, but unfortunately the pandemic put the trial on pause for a number of months. However, by the end of 2020 recruitment was restored, and initial dosing began in several countries in Europe, including in the UK. This progressed throughout 2021.

Drug repurposing

2020 was the third year of our 3-year drug repurposing research grant to Dr James Dowling at the Hospital for Sick Children, Toronto, Canada. One of the aims of this grant was to determine the optimum dosage of Tamoxifen to take to clinical trial. By the end of 2020 this work had progressed successfully enough for clinical trial planning to be well advanced in sites in Canada, the US, and the UK (see grant announcement below).

Drug repurposing has the benefit of bringing drugs that have already been safely taken by thousands, maybe millions of other people, to a new group of patients. As safety has already been established, the length of clinical trial required to test such a drug for a new patient group, and the proof required for the regulatory authorities, can be much reduced. Patients, particularly those already living with a high degree of vulnerability, may also feel a lot more confidence and faith in a known drug.

On the road to all these clinical trials, the role of the Trust was to fund the proof of principle/validation work being proposed by these outstanding researchers, paving the way for companies like Astellas Gene Therapies and Dynacure, or academic institutions such as Sick Kids Toronto and Great Ormond St. London, to take them to clinical trial. That funding makes a fundamental difference, and we are immensely grateful to all our supporters who have made this possible.

We are also immensely grateful to our Scientific Advisory Board (SAB) for their time and their highly impressive expertise and understanding. The calibre of applications the Myotubular Trust attracts is due in no small part to the reputation of this group of scientists.

The academic members of the SAB are:

- Professor Francesco Muntoni, Head of the Dubowitz Neuromuscular Centre, Great Ormond Street Hospital
- Dr Meriel McEntagart, Consultant Clinical Geneticist, St. George's Hospital, London
- Professor Michael Duchon, Professor of Physiology, University College London
- Dr Susan C Brown, previously Reader in Translational Medicine, Department of Veterinary Basic Science, Royal Veterinary College, University of London
- Professor Volker Straub, Harold Macmillan Professor of Medicine, Consultant in Neuromuscular Genetics and Paediatrics, Newcastle University
- Professor Dominic Wells, Professor in Translational Medicine, Royal Veterinary College

We are indebted for the guidance they gave to the Myotubular Trust throughout the year. We are also very grateful to the lay members of our SAB for their time. The lay members include parents, bereaved parents and patients.

TRUSTEES' ANNUAL REPORT 31 December 2021

Financial Review

Sustainable Fundraising – the Highlights of 2021

In 2021 the Trustees were gratified that we were able raise £144,770, despite pandemic related challenges still fundamentally impacting charity fundraising. Our continued revenue stream is testament to the strength of support that a small number of affected families enjoy in their communities – the 'ripple effect' from each child into an extended network of supporters has been so critical to our growth and stability.

Despite the year that was in it, our families were able to organise the now famous Jack Blunsdon annual golf tournament – in its 15th year! – and Monte's Golf Cup had its inaugural event. Young Rian organised his own 100K Wheel sponsored event, and many other families took part in virtual fundraisers and sponsored events such as the 2021 virtual 10K.

Sadly, 2021 was a year of many losses and we extend our gratitude to the families and friends of those boys who in their time of grief considered the Myotubular Trust for donations.

We were fortunate to be supported by Jeans 4 Genes and the Edward Gosling Foundation, as well as Global's Make Some Noise and IGY Foundation continued support. We thank them all for their financial and moral support. Thank you for seeing the value of the work we do.

Once again we had an increase in standing orders during 2021, probably as people realised how difficult it was for charities during social distancing and lockdowns. Thank you to you all.

Fundraising Practice

The Trustees take their responsibilities to fundraising very seriously. To that end, we ensure that we adhere to the Fundraising Regulator's code of best practice and meet the Charity Commission's six principles of charity fundraising. For us, at our size, the areas of best practice we pay attention to are;

- providing information on how to fundraise safely,
- considered communication with all fundraisers, which is appropriate to our strategy,
- carrying out a proportionate process of due diligence around fund raising proposals,
- making a record of the issue and return of any charity collection materials,
- securing cash donations and banking them as soon as possible,
- not sharing personal data without explicit consent,
- including opt-out information on fundraising communications sent to a named individual,
- processing unsubscribe requests in a timely way,
- using funds as they have been directed by specific donors, in particular allocating restricted funds appropriately.

We adhere to the Data Protection Act 2018, General Data Protection Regulation (GDPR) and pay data protection fees to the Information Commissioner's Office (ICO).

TRUSTEES' ANNUAL REPORT 31 December 2021

Reserves Policy

The Trustees sole aim in expending cash reserves is to fund research into a cure or treatment for myotubular myopathy and they do not consider it appropriate to hold long-term reserves.

However, as each research project is granted, those funds will be held available to be released in staged payments, and new awards will only be made if the full cost of the relevant research project is available, and available to be ringfenced. This prudent financial policy is appropriate given our size and specialism.

This policy meant that instead of being hit by a cash flow crisis in 2020 and 2021, and the even worse possibility of not being able to pay for committed research grants, we were even able to announce new grant awards in 2020, announce another grant call for 2021 and prepare to announce another call in 2022.

Plans for future periods

The Trust aims in 2022 to:

- Maintain excellence in family support, advocacy, information provision, and continue to make the introductions that families tell us are invaluable.
- Launch the Care Hours Survey as an academically led study with full ethical approval.
- Announce our 13th grant call.
- Maintain the impetus behind the Liver Discussion WorkGroup and seek ways to influence the vital progression of work to understand the implications of liver issues in myotubular myopathy.
- Continue to work with key stakeholders in the neuromuscular disease community, and strategic rare disease organisations.
- Continue to work with regulatory authorities – particularly the MHRA in the UK - on behalf of patients with myotubular and centronuclear myopathy.
- Plan ahead and prepare effectively for any future NICE review of treatments for myotubular and centronuclear myopathy, facilitating families' and patients' input.
- Partner with and support TREAT-NMD on the long-term excellence and sustainability of the Myotubular and Centronuclear Myopathy Patient Registry.
- Continue to share information with, and promote collaboration between, other family and patient organisations, relevant scientific interest groups and research organisations.
- Continue to secure separate funding to cover the Trust's running costs.
- Maintain our 2021 support of fundraising events, despite the continued challenges brought about by the pandemic.

TRUSTEES' ANNUAL REPORT 31 December 2021

Reference and administrative details of the Charity, its Trustees and advisors

The following were Trustees of the Trust and held office during the above period:

Patricia Allen
Gary Browning
Greg Fowler
Andrew Lennox
Anne Lennox
James Rosling

Trustees are appointed by the board of trustees and serve for three years (five years for Anne Lennox) after which period they may put themselves forward for re-appointment. The trustees meet three times per annum.

Office

Myotubular Trust

- charity registration number 1137177
- company registration number 07260229

15a Barnard Road
London SW11 1QT

Bankers

CAF Bank Limited
Kings Hill
West Mailing
Kent
ME19 4JG

The Co-operative Bank
PO Box 250
Skelmersdale
WN8 6WT

Independent Examiner

Michael Stone MA ACA
Jamieson Stone LLP
Windsor House
40/41 Great Castle Street
London
W1W 8LU

Structure, Governance and Management

Constitution

The Myotubular Trust is an incorporated charity limited by guarantee and its governing document is the memorandum and articles of association dated 21 May 2010. The memorandum and articles of association has the same objects as that of the Trust Deed dated 26 January 2006 of the unincorporated charity. The Trust obtained charitable status under Section 4 of the Charities Act 1960 from the Charity Commission on 19 April 2006 under registration number 1113809 and following incorporation on the 20th May 2010 was registered with the Charity Commission with registration number 1137177, and with Companies House with company registration number 7260229.

Organisation and the Trustees

In selecting individuals for appointment, the trustees will have regard to the skills, knowledge and experience needed for the effective administration of the charity.

TRUSTEES' ANNUAL REPORT 31 December 2021

Trustees' responsibilities statement

The Trustees (who are also directors of The Myotubular Trust for the purposes of company law) are responsible for preparing the Trustees' Report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards.

Company law in England and Wales requires the Trustees to prepare financial statements for each financial year in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards and applicable law). The financial statements are required by law to give a true and fair view of the state of affairs of the charity and of the income and expenditure of the charity for that period. In preparing these financial statements the trustees are required to:

- Select suitable accounting policies and then apply them consistently
- Observe the methods and principles of the Charities SORP
- Make judgments and estimates that are reasonable and prudent
- State whether applicable UK accounting standards have been followed and statements of recommended practice, subject to any departures disclosed and explained in the financial statements and
- Prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue to operate.

The trustees are responsible for keeping accounting records, which disclose with reasonable accuracy at any time the financial position of the charity and enable them to ensure that the financial statements comply with the Companies Act 2006. They are responsible for safeguarding the assets of the charity and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

Risk management

The trustees have examined the strategic, business and operational risks, which the charity faces and confirm that systems have been established to enable regular reports to be produced so that the necessary steps can be taken to lessen the risks.

INDEPENDENT EXAMINER'S REPORT FOR THE YEAR ENDED 31 DECEMBER 2021

Respective responsibilities of trustees and examiner

The trustees (who are also the directors of the company for the purpose of company law) are responsible for the preparation of the accounts. The charity's trustees consider that an audit is not required for this year under section 144 of the Charities Act 2011 (the Charities Act) and that an independent examination is needed.

Having been satisfied that the charity is not subject to audit under company law and is eligible for independent examination it is my responsibility to:

- examine the accounts under section 145 of the Charities Act,
- to follow the procedures laid down in the General Directions given by the Charity Commission (under section 145(5)(b) of the Charities Act, and
- to state whether particular matters have come to my attention.

Basis of independent examiner's statement

My examination was carried out in accordance with the General Directions given by the Charity Commission. An examination includes a review of the accounting records kept by the charity and a comparison of the accounts presented with those records. It also includes consideration of any unusual items or disclosures in the accounts, and the seeking of explanations from you as trustees concerning any such matters. The procedures undertaken do not provide all the evidence that would be required in an audit, and consequently, no opinion is given as to whether the accounts present a 'true and fair view' and the report is limited to those matters set out in the statement below.

Independent examiner's statement

In connection with my examination, no matter has come to my attention:

- 1) which gives me reasonable cause to believe that in, any material respect, the requirements:
 - to keep accounting records in accordance with section 130 of the Charities Act; and
 - to prepare accounts which accord with the accounting records and to comply with the accounting requirements of the Companies Act 2006 and with the methods and principles of the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2015) have not been met; or
- 2) to which, in my opinion, attention should be drawn in order to enable a proper understanding of the accounts to be reached



Michael Stone MA ACA
Jamieson Stone LLP
Windsor House
40/41 Great Castle Street
London
W1W 8LU

16 September 2022

STATEMENT OF FINANCIAL ACTIVITIES FOR THE YEAR ENDED 31 DECEMBER 2021

	Unrestricted Funds £	Designated Funds £	Restricted Funds £	Total Funds 2021 £	Total Funds 2020 £
<u>INCOMING RESOURCES</u>					
Donations and grants	58,503	42,500	-	101,003	110,628
Fundraising activities	43,028	-	-	43,028	20,635
Interest received	739	-	-	739	1,602
	-----	-----	-----	-----	-----
Total incoming resources	102,270	42,500	-	144,770	132,865
	-----	-----	-----	-----	-----
<u>RESOURCES EXPENDED</u>					
Research	-	41,289	-	41,289	133,306
Fundraising costs	464	-	-	464	345
Outreach work	-	2,500	-	2,500	-
Staff costs	49,961	-	-	49,961	50,765
Training	719	-	-	719	-
Advocacy	-	13,000	-	13,000	12,187
Family Conference costs	150	-	-	150	-
Accountancy & payroll	140	-	-	140	110
Independent examiner	1,000	-	-	1,000	1,000
Legal & professional	445	-	-	445	-
Trustee's indemnity	873	-	-	873	966
Travel costs	-	-	-	-	216
Printing & stationery	89	-	-	89	72
Postage & telephone	11	-	-	11	56
Subscriptions	174	-	-	174	260
Web & IT costs	1,497	-	-	1,497	688
Bank charges	214	-	-	214	300
Miscellaneous costs	104	-	-	104	-
	-----	-----	-----	-----	-----
Total resources expended	55,841	56,789	-	112,630	200,271
	-----	-----	-----	-----	-----
Net incoming/(outgoing) resources	46,429	(14,289)	-	32,140	(67,406)
Transfers between funds	(45,690)	45,690	-	-	-
	-----	-----	-----	-----	-----
Net movement in funds	739	31,401	-	32,140	(67,406)
	-----	-----	-----	-----	-----
Total funds brought forward	5,962	289,041	-	295,003	362,409
	-----	-----	-----	-----	-----
Total funds carried forward	6,701	320,442	-	327,143	295,003
	-----	-----	-----	-----	-----

All gains and losses arising in the year are included within the statement of financial activities

The accompanying notes form part of these financial statements

Myotubular Trust

BALANCE SHEET AS AT 31 DECEMBER 2021

	£	2021 £	£	2020 £
CURRENT ASSETS				
Debtors and prepayments	25,419		26,275	
Cash at bank and in hand	303,447		270,455	
	-----		-----	
Total current assets	328,866		296,730	
	-----		-----	
CREDITORS				
Amounts falling due within one year	1,723		1,727	
	-----		-----	
Net current assets		327,143		295,003
		-----		-----
NET ASSETS		327,143		295,003
		-----		-----
FUNDS OF THE CHARITY				
Restricted funds		-		-
Unrestricted general funds		6,701		5,962
Unrestricted designated funds		320,442		289,041
		-----		-----
		327,143		295,003
		-----		-----

The company is entitled to exemption from audit under Section 477 of the Companies Act 2006 for the year ended 31 December 2021 and the members have not required the company to obtain an audit of its financial statements for the year ended 31 December 2021 in accordance with Section 476 of the Companies Act 2006.

The directors acknowledge their responsibilities for: (a) ensuring that the company keeps accounting records which comply with Sections 386 and 387 of the Companies Act 2006 and (b) preparing financial statements which give a true and fair view of the state of affairs of the company as at the end of each financial year and of its profit or loss for each financial year in accordance with the requirements of Sections 394 and 395 and which otherwise comply with the requirements of the Companies Act 2006 relating to financial statements, so far as applicable to the company.

The financial statements have been prepared in accordance with the provisions of Part 15 of the Companies Act 2006 relating to small companies.

The financial statements were approved by the trustees on and signed on their behalf:



.....
Andrew Lennox
Chairman/Trustee



.....
James Rosling
Treasurer/Trustee

The accompanying notes form part of these financial statements

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2021

1. BASIS OF PREPARATION

The financial statements have been prepared on the accruals basis of historic cost in accordance with the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2015) and the Companies Act 2006 and the Charities Act 2011.

2. ACCOUNTING POLICIES

Incoming resources

Incoming resources are recognised when the charity becomes entitled to the resources, the trustees are virtually certain they will receive the resources, and the monetary value can be measured with sufficient reliability.

Where incoming resources have related expenditure (as with fundraising or contract income) the incoming resources and related expenditure are reported gross in the Statement of Financial Activities.

Grants and donations are recognised when the charity has unconditional entitlement to the resources.

Incoming resources from tax reclaims are recognised at the same time as the gift to which they relate.

Contractual income and performance related grants are recognized once the related goods or services have been delivered.

Investment income is included in the accounts when receivable.

Resources expended

Resources expended are recognised as soon as there is legal or constructive obligation committing the charity to pay out resources.

Resources expended include attributable VAT which cannot be recovered.

Funds

Restricted funds are funds to be used for specific purposes as declared by the donor.

Designated funds are monies set aside from general funds and designated for specific research awards by the trustees.

Unrestricted funds are donations and all other incoming resources without a specified purpose and which are available as general funds.

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED)

FOR THE YEAR ENDED 31 DECEMBER 2021

3. TAXATION

The Myotubular Trust is a registered charity and is not liable to Income Tax or Corporation Tax on income derived from its charitable activities.

4. RESOURCES EXPENDED

	2021 £	2020 £
Research	41,289	133,306
Independent examiner's remuneration	1,000	1,000
	-----	-----

The principal research grants awarded during the year were as follows:

	2021 £	2020 £
Hnia at Inserm	29,059	-
Tamoxifen Protocol	2,469	-
Newcastle University re Treat NMD	7,500	-
Research Consultancy	2,261	-
Sick Kids Canada - Dr Dowling	-	72,000
Sparks Charity GOSH	-	58,108
Taurus Tide	-	3,198
	-----	-----

5. DEBTORS AND PREPAYMENTS

	2021 £	2020 £
Gift Aid	419	133
Prepayments and accrued income	25,000	26,142
	-----	-----
	25,419	26,275
	-----	-----

6. CREDITORS FALLING DUE WITHIN ONE YEAR

	2021 £	2020 £
Accruals	1,723	1,727
	-----	-----

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED) FOR THE YEAR ENDED 31 DECEMBER 2021

7. RELATED PARTY TRANSACTIONS

There were no related party transactions by the trustees for the year (2020: None).

One Trustee received remuneration of £20,000 during the year ending 31 December 2021 (2020: £20,000).

The trustee's remuneration and other administration costs are funded from unrestricted corporate and charitable donations, which were specifically raised for that purpose.

MYOTUBULAR TRUST

England & Wales - Charity number 1137177

Accounts



Annual Report and Financial Statements

To the year ended
31 December 2020



TRUSTEES' ANNUAL REPORT 31 December 2020

TRUSTEES' ANNUAL REPORT 31 December 2020

The Trustees of the Myotubular Trust take pleasure in presenting their annual report and the financial statements for the year ended 31 December 2020.

Objects and Activities

The objects of the Myotubular Trust as agreed by the Charity Commission are;

- the relief of disability and the extension of life for babies, children and adults suffering from myotubular myopathy,
- by promoting the study of, and research into, the treatment and cure of the muscle weakness caused by myotubular myopathy.

The Trust, its Trustees, staff and many volunteers all focus on five outcomes to enable the achievement of these objectives:

1. Bringing families together
2. Promoting and funding international research
3. Sharing knowledge
4. Promoting innovative thinking and collaboration
5. Working with our extended families.

We bring about the public benefit required of all charities, by the activities of:

- making grants to organisations and individuals.
- providing advocacy, advice, and information.
- sponsoring research.

Myotubular Myopathy and Centronuclear Myopathy

Myotubular myopathy is a rare and extremely life-threatening muscle condition, which causes profound muscle weakness, usually from birth. It is one of a group of conditions called centronuclear myopathies – called this because under a microscope the nucleus of the muscle cell of someone affected is in the centre, rather than at the edge of the cell.

These conditions are genetic in inheritance. The gene mutation for x-linked myotubular myopathy is carried on the x chromosome (xlmtm), and is the most common form, affecting (mainly) boys. They usually do not survive their babyhood – the statistics have been under review in the last few years and the current view is that 50-75% die in their first year, and very few make it to adulthood.

Even rarer genetic forms, either dominant or recessive in inheritance, can affect both males and females, boys and girls and are generally milder in severity, although not always. The terms myotubular and centronuclear myopathy both describe 'our' condition.

Children and adults with myotubular myopathy often require vigilant nursing care, ventilators to breathe, power wheelchairs to get around, and are usually fed via a tube into the stomach. Carrier females, and those affected by some of the rarer forms which can manifest in adult life, may develop muscle weakness and problems with eating and drinking; walking and movement; muscle fatigue and susceptibility to respiratory weakness and associated infections.

In 2020, three young boys who were taking part in the gene therapy trial for x-linked myotubular myopathy tragically died. We would like to take this opportunity to extend the deepest sympathies of the Myotubular Trust to their families and those who loved and took care of them.

TRUSTEES' ANNUAL REPORT 31 December 2020

Impact of COVID-19: Uncertain times

The impact of the global pandemic on the myotubular and centronuclear myopathy patient community was undoubted. This group of patients was identified as '**at risk of severe illness if they catch Coronavirus**' and were generally advised to shield. The effect of this new virus on those with a neuromuscular condition was of course unknown at the outset and it was a hugely concerning time. Happily, the severity of the disease did not seem to be worsened for our group of patient and we did not experience an increased death rate due to Covid19.

The initial NHS response in the UK to our patients and families regarding advice was very thorough. Families and individuals felt that they were provided with good signposting and helpful information around shielding, accessing emergency food and medicines.

However, there were a myriad of other ways in which the myotubular and centronuclear myopathy patient and family community were affected by the pandemic in 2020 including;

- Delays with planned routine treatments and health screening.
- Postponement of surgical interventions, which while not immediately urgent, were vital.
- Complexities, and profound delays, in discharge from hospital for new babies.
- An increased care load for parent caregivers who either chose, for safety reasons to cease having carers and nurses come into the home, or whose carers were unable to work (due to homeschooling their own children; self-isolation requirements; lack of PPE; risk of cross contamination between their caseloads).
- Getting sufficient respiratory related medical supplies and getting hold of PPE in the first months.
- A shortage of skilled agency staff with in-depth respiratory and ventilation training.
- Lack of clear guidelines about ventilated children returning to school – often meaning they could not go back with their classmates.
- Ongoing anxiety about mixing socially, and therefore increased isolation for an already isolated group.
- The pausing of clinical trials and studies – for a disease which has waited a very long time for any human clinical trials.

"We lost a few nurses due to COVID related complications in their own lives. So now I step in to fill the gaps, and lack of sleep has been a big issue in terms of holding it together."

"My son was happy staying home during lockdown, and we have struggled getting him out and about since - he wants to stay home and do home schooling and play with his Wii. His big sister struggled going back to work and had big anxieties about bringing Covid home to her brother. I had to quit my job because of fear of getting Covid and bringing it home."

"My husband and I got Coronavirus at the same time, and I was so scared that my son's carers would walk away. But actually, they were amazing and increased their working hours."

The Myotubular Trust responded to the pandemic related needs of our community by:

- Offering all the support we would normally have provided in person by phone and conference call facility, including sometimes training families in the use of online tools.
- Ensuring that the most up to date information for those living with NMD was available on the website as soon as it became available.
- Organising Zoom Family meetings - covering topics including research updates, studies on carrier women and mental health and well-being, delivered by a range of professional experts and neuromuscular scientists and clinicians.
- Finding online fundraising events for those who wanted to fundraise or wanted to have a goal for activity.

TRUSTEES' ANNUAL REPORT 31 December 2020

Achievements and Performance

Myotubular Trust is now 15 years old, and we are gratified to find that we continue to make a real and meaningful difference, even in remarkably unprecedented times. There is clearly a very useful role for a disease specific research funder in the world of rare disease, along with a tangible need to support patients and families

The Trust was established in 2006 by two parents of boys with myotubular myopathy, to raise research funds. We had found that there was no other way for passionate parents to ring-fence money to fund research into a treatment or cure for this condition, even though we did at the time approach some larger charities for whom we had hoped to fundraise. We also realised very quickly that it was essential to support the profile of the condition within the neuromuscular research community – to compete for brains and innovative ideas – and to support those living with, and bereaved by, myotubular myopathy.

When Myotubular Trust was established, we hoped to be able to fund one or two substantial pieces of research. We hoped that we would help establish proof of principle in one or two key areas, perhaps fund research to start to answer certain important unknowns and 'compete for brains' in a field where it was clear that breakthroughs were on the horizon.

Little did we realise that the Trust would still be a viable fundraising and funding resource 15 years later; how we would be the charity that funded the proof of principle research that led to the first ever clinical trial for x-linked myotubular myopathy; how many different and fundamental research possibilities would open up; how many families would come together to provide support for each other; how much we would see myotubular and centronuclear myopathy push ahead of other rare neuromuscular diseases in bringing research to pre-clinical studies and clinical trial; and finally ...how we would see the charity and community through a global respiratory pandemic.

Since founding 15 years ago...we have:

1. Raised **£2.4M**, through family-led fundraising, networks and relationships.
2. Made **16 research grants** to researchers in world class laboratories, with the support of a highly regarded Scientific Advisory Board.
3. Funded the proof of principle project for gene therapy that led to the **first ever clinical trial** for myotubular myopathy which began in the autumn of 2017.
4. Funded **other proof of principle projects** that are on track to lead to clinical trials.
5. Funded two research grants that contributed to the discovery of **two new genes** implicated in centronuclear and myotubular myopathy.
6. Hosted **five family conferences**, bringing together affected individuals and families, researchers, clinicians, and other health professionals, and arranged more family meetings by **Zoom during the pandemic with global experts and scientists**.
7. Created the first disease specific international **Patient Registry** to gather vital information on the condition and funded its migration to the stability and credibility of a university setting.
8. Sponsored a **Standards of Care** meeting for clinicians, patients and their healthcare professionals at the Royal Brompton Hospital.
9. Participated in a European Neuromuscular Centre workshop on Mouthpiece Ventilation, resulting in the publication of **MPV international best practice guidelines**.
10. Created a great band of **committed supporters**, raising funds for us year on year.
11. Developed strategic relationships with **key stakeholders** in the fields of neuromuscular disease, rare disease, EU and UK regulatory bodies, and highly regarded well-established UK children's charities.
12. And **most importantly**, brought together more and more families affected by myotubular and centronuclear myopathy, supporting the Trust's fundraising and each other's lives.

TRUSTEES' ANNUAL REPORT 31 December 2020

Family Support in 2020

Advocacy and Family Support

We were very fortunate that since 2016-2017 we have received annual grants from IGY Foundation to enable us to support families and to help with professional advice on respiratory issues, ventilatory support, applications for home services and adaptations, school support etc. This service was invaluable in the challenging year 2020.

As a reminder of why this support is needed, myotubular myopathy is so rare that usually the child's GP or doctor will never have come across the condition before - making being diagnosed a frightening and bewildering experience for all concerned. Being hurled suddenly and without warning into a world of medical jargon, high level nursing, complex healthcare and social care systems, families and individuals are grateful to know they are not alone, and that we, and others like them, are willing to share the burden of responsibility by helping them understand their experiences and to navigate the systems. For example:

- At a time when parents are supposed to be celebrating the birth of an infant, our families are often instead in the position of having to make important choices around giving their child the best quality of life, and a chance of longer-term survival. The information these families are given to make those decisions is sometimes inaccurate, often patchy, and even delivered by someone who has never seen a child with the condition before.
- When a baby is finally stable enough to go home, it is not unusual for the transition process to take 1 year to 18 months. There are huge differences between the capability of different hospitals, different clinical commissioning groups, and different community nursing support services in making this happen in a timely fashion. This was further complicated in 2020 by the challenges of bringing together the multi-disciplinary teams necessary for this complex step, and the high demand for respiratory and ventilatory trained agency staff.
- Parents also have a desperate need for encouragement, reassurance, and practical support to feel comfortable with their new parent caregiving roles quickly, to help them better understand the nuances of the condition and to help them to feel more 'in control'.
- Local medical teams, who are quite likely seeing their first ever baby with myotubular myopathy, need support with information and access to specialist advice and support - such as what equipment to provide the family and what the optimal settings may be on breathing equipment.

The need caused by a lack of understanding of the impacts of such a rare, devastatingly life threatening condition re-emerges many times throughout a patient's life - and more often at times of change, such as when there is a physical change (such as losing the ability to walk or scoliosis), during periods of ill health, when moving home or into a new phase of education or work, around family planning, or practical day-to-day living issues. So often experiences and information signposting are needed again and again by families.

We were very glad to be able to provide this support to many families again in 2020 despite the challenges of a global pandemic.

TRUSTEES' ANNUAL REPORT 31 December 2020

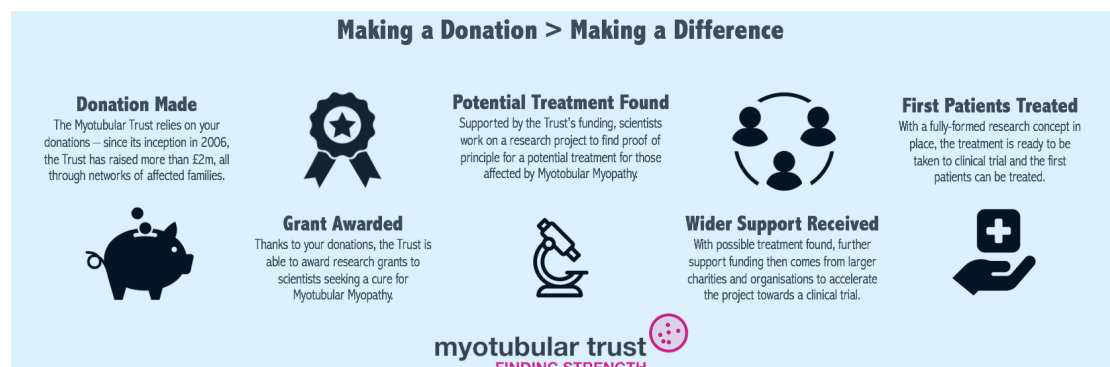
Case study

The advice given to the parents of a 2 year old boy with myotubular myopathy has had a huge influence on how they manage his airways to keep him safe. In the early days, when the baby was unable to cope with the volume of secretions and he wasn't strong enough to swallow, we drew his parent's attention to nasal suctioning, chest physiotherapy and nebulisers. This was at a point when their hospital was not putting these steps in place as they were unfamiliar with the condition. Myotubular Trust also advocated for the family to use a cough assist device, which is now an integral part of the boy's physiotherapy routine - this has strengthened his cough and improved his ability to clear his secretions independently. This is all second nature to his parents now, and together with the night-time nursing care package that the Trust helped to put in place, his parents believe that the airways management regime is the reason their son has avoided chest infections and lengthy hospital admissions in the first two years of his life. They say that it is also why, at the age of 3, he is strong enough to attend nursery, just like any other little boy his age.

"Myotubular Trust has been there, and will continue to be there, at every stage of this journey we are on, to support us and improve his life experience and that is incredibly comforting and reassuring to us as parents. I really couldn't ever state this enough!!"

Research in 2020

The Myotubular Trust was set up to raise funds to leverage the research findings being made, and techniques being trialed in 'more common' muscle diseases. The ultimate goal of the Trust is to invest in a diverse number of routes to a cure for all genetic forms of myotubular and centronuclear myopathy, or in treatments that alleviate the most severe symptoms. This we do by investing in the very best translational research, peer reviewed to the highest international standards, supported by an eminent Scientific Advisory Board.



Proof of principle funding

The founding vision for the Trust was to fund proof of principle projects that would not normally be funded by public or industrial funding. For rare diseases it can be incredibly difficult to finance this vital stage of research, but once proof of principle is established for a potential treatment, then other larger charities and organisations are more likely to provide funds for the next stage. We had great hopes that this strategy might make some difference for our very rare disease, and we are gratified that all three current promising clinical trials for treatments have had significant early-stage funding from Myotubular Trust.

TRUSTEES' ANNUAL REPORT 31 December 2020

Clinical trials

Gene therapy

This virus mediated gene therapy was being funded by the Trust as far back as our first grant award in 2009 to Dr Ana Buj Bello at Genethon, Paris. Dr Buj Bello established proof of principle for this gene therapy, and with the success of her research funded by the Trust (grants in 2009 and 2012), other funders subsequently joined in too. *"It is the result of perseverance and joined forces. Thanks a lot for your support all along these years, your contribution has been crucial, you can be proud of it"* Dr Buj Bello

This trial reached its 3 year mark in 2020, but tragically and devastatingly 3 young boys died, probably due to liver complications. The trial was put on hold by the FDA in the US for most of 2020, and after some months of reporting by the sponsoring company (previously Audentes Therapeutics, now part of Astellas Gene Therapies), the hold was lifted again in December. In 2021 it is expected that dosing will resume, at a lower dose than that given to the deceased boys.

Antisense Therapy

The 3year grant, *"Reducing DNM2 as a novel therapeutic target for CNM"*, made by the Myotubular Trust to Jocelyn Laporte's team at the laboratory IGBMC in 2016 *"validated a deliverable approach"*, and formed a major contribution to the pre-clinical studies preparing the way for a clinical trial to test this approach in humans—who have either the x-linked MTM or Dynamin 2 form of the condition.

In 2019, Dynacure, a start-up biotech based in Strasbourg, secured approval for a clinical trial for those affected by the MTM1 and DNM2 genes, and this trial was due to begin in 2020. One patient began treatment, but unfortunately the pandemic put the trial on pause for a number of months. However, by the end of 2020 recruitment was restored, and initial dosing began in several countries in Europe, including in the UK.

Drug repurposing

2020 was the third year of our 3-year drug repurposing research grant to Dr James Dowling at the Hospital for Sick Children, Toronto, Canada. One of the aims of this grant was to determine the optimum dosage of Tamoxifen to take to clinical trial. By the end of 2020 this work had progressed successfully enough for clinical trial planning to be well advanced in sites in Canada, the US, and the UK (see grant announcement below).

Drug repurposing has the benefit of bringing drugs that have already been safely taken by thousands, maybe millions of other people to a new group of patients. As safety has already been established, the length of clinical trial required to test such a drug for a new patient group, and the proof required for the regulatory authorities, can be much reduced. Patients, particularly those already living with a high degree of vulnerability, may also feel a lot more confidence and faith in a known drug.

This now brings **the number of clinical trials** for centronuclear and myotubular myopathy to **three**, all of which have had substantial investment and commitment from Myotubular Trust. On the road to all of these clinical trials, the role of the Trust was to fund the proof of principle/validation work being proposed by these outstanding researchers, paving the way for companies like Audentes (now Astellas Gene Therapies) and Dynacure, or academic institutions such as Sick Kids Toronto and Great Ormond St. London to take them to clinical trial. That funding makes a fundamental difference, and we are immensely grateful to all our supporters who have made this possible.

TRUSTEES' ANNUAL REPORT 31 December 2020

Grant awards – 2020

In 2020, despite the challenging fundraising and financial position of charities throughout the UK, we were in the fortunate position to be able to make two research grants:

Tamoxifen clinical trial

This grant, which is co-funded with Great Ormond Street Hospital Children's Charity, is for the UK arm of a clinical trial to test how well the well-known oncology drug, Tamoxifen, works in improving motor and respiratory function in patients with myotubular myopathy. The trial will be led by Dr Giovanni Baranello, and Professor Francesco Muntoni at the UCL Great Ormond Street Institute of Child Health. It will involve children affected by x-linked myotubular myopathy in the UK and is part of the global repurposing trial from the work the Trust funded with Dr Jim Dowling at Sick Kids Canada. The global trial is being led by Dr Dowling.

The mTORC pathway

Our second grant award of 2020 went to **Dr Karim Hnia** at the world-renowned French institute, INSERM, investigating the question "Is the mTORC1 pathway a route to treatment in x-linked myotubular myopathy?"

mTORC1 is a master regulator of muscle growth – from the early steps of muscle cell differentiation in the womb, to the work of muscles in adult life. The work of Dr Hnia's laboratory has shown that mTORC1 is 'overactivated' when XLMTM is present. What makes this a very interesting project (apart from the highly positive peer review) is that through other diseases there are a number of drugs already licensed to regulate mTORC1 levels.

Another important goal in being a source of funding for this condition was to inspire others in the field to work on myotubular and centronuclear myopathy in order to develop a sustainable legacy of research for our condition. Fourteen years later we are delighted to be supporting a committed community of researchers with an interest in myotubular myopathy, undertaking world-class research projects.

We are also immensely grateful to our Scientific Advisory Board (SAB) for their time and their highly impressive expertise and understanding. The calibre of applications the Myotubular Trust attracts is due in no small part to the reputation of this group of scientists.

The academic members of the SAB are:

- Professor Francesco Muntoni, Head of the Dubowitz Neuromuscular Centre, Great Ormond Street Hospital
- Dr Meriel McEntagart, Consultant Clinical Geneticist, St. George's Hospital, London
- Professor Michael Duchon, Professor of Physiology, University College London
- Dr Susan C Brown, previously Reader in Translational Medicine, Department of Veterinary Basic Science, Royal Veterinary College, University of London
- Professor Volker Straub, Harold Macmillan Professor of Medicine, Consultant in Neuromuscular Genetics and Paediatrics, Newcastle University
- Professor Dominic Wells, Professor in Translational Medicine, Royal Veterinary College

We are indebted for the guidance they gave to the Myotubular Trust throughout the year. We are also very grateful to the lay members of our SAB for their time. The lay members include parents, bereaved parents and patients.

TRUSTEES' ANNUAL REPORT 31 December 2020

Partnerships

With the goal of collaboration and innovation in mind, we continued in 2020 to work with key stakeholders in the research, children's charity, industry, regulatory and myotubular myopathy communities:

- The research charity of the world-renowned children's hospital, Great Ormond Street, again invited us to partner with them to issue a joint grant call for translational research into myotubular and centronuclear myopathy, and together we are jointly funding a clinical trial to examine the effect of Tamoxifen on the symptoms of x-linked myotubular myopathy.
- We took part in the creation and promotion of a European study, led by the University of Essen, into symptoms of muscle disease in female carriers and relatives of boys with x-linked myotubular myopathy. This study was initiated at the Family Meeting of the German patient organization ZNM – Zusammen Stark e.V.
- We supported the communications of the centronuclear myopathy voluntary organisation, The Information Point.
- We supported lobbying initiatives by MDUK, Genetic Alliance UK and Rare Disease UK in parliamentary meetings.
- We contributed to meetings of the Patient Group Consultative Forum of the UK Medicine and Healthcare Products Regulatory Agency (MHRA).
- We continued to engage in learning and dialogue about Highly Specialised Technologies with NICE, the UK public body which provides advice and guidance on new medicines to be adopted by the NHS.
- We continued to work closely with organisations in the biotech field who are focusing on myotubular myopathy; the TREAT-NMD's Registry team; and with corporate backers who provide us with pro bono services or grants for running the Trust.

Given our relatively small size, these partners are crucial for us and we value their time and commitment immeasurably, and hope we can continue to be excellent partners with them.

TRUSTEES' ANNUAL REPORT 31 December 2020

Financial Review

Sustainable Fundraising – the Highlights of 2020

In 2020 the Trustees were gratified that we were able to raise £131,865, despite the remarkably unprecedented times impacting charity fundraising. Our continued revenue stream is testament to the strength of support that a small number of affected families enjoy in their communities – the 'ripple effect' from each child into an extended network of supporters has been so critical to our growth and stability.

Despite the year that was in it, our families were able to organise

- The 14th Jack Blunsdon annual golf tournament – with full social distancing
- Two 10K runs
- A half marathon
- Several events to support the 2.6 Challenge – a virtual fundraising call to action, arranged by the organisers of the London Marathon, suggesting that people raise money for charities by creating any event that involved the numbers 2 and 6 (in recognition of the length of a normal marathon)
- In memoriam donations
- Online shopping and eBay donations
- As well as a range of 10K runs, Hope Walks, Tough Mudders, a very impressive London Marathon run and a first ever Manchester Marathon.

We also had an increase in standing orders during 2020, probably as people realised how difficult it was for charities during social distancing and lockdowns. Finally, we were incredibly fortunate that JCW Resourcing, an IT recruitment company, chose the Myotubular Trust as the recipient of their annual January fundraising event, in recognition of the lovely son of one of their colleagues. This provided us with a very welcome £30K+ start to our fundraising in 2020 - little did we know then how vital that would be.

We were also lucky to be chosen by the charity, Global's Make Some Noise for emergency Covid funding. Their process was very thoughtful and considerate, and we really felt that there were organisations out there rooting for small charities like ours.

We would also like to extend our grateful thanks to the IGY Foundation for their continued support of our family support work – we are truly grateful to them for both the funds, and for the interest in, and understanding of this work we do.

Fundraising Practice

The Trustees take their responsibilities to fundraising very seriously. To that end, we ensure that we adhere to the Fundraising Regulator's code of best practice and meet the Charity Commission's six principles of charity fundraising. For us, at our size, the areas of best practice we pay attention to are;

- providing information on how to fundraise safely,
- considered communication with all fundraisers, which is appropriate to our strategy,
- carrying out a proportionate process of due diligence around fund raising proposals,
- making a record of the issue and return of any charity collection materials,
- securing cash donations and banking them as soon as possible,
- not sharing personal data without explicit consent,
- including opt-out information on fundraising communications sent to a named individual,
- processing unsubscribe requests in a timely way,
- using funds as they have been directed by specific donors, in particular allocating restricted funds appropriately.

We adhere to the Data Protection Act 2018, General Data Protection Regulation (GDPR) and pay data protection fees to the Information Commissioner's Office (ICO).

TRUSTEES' ANNUAL REPORT 31 December 2020

Reserves Policy

The Trustees sole aim in expending cash reserves is to fund research into a cure or treatment for myotubular myopathy and they do not consider it appropriate to hold long-term reserves.

However, as each research project is granted, those funds will be held available to be released in staged payments, and new awards will only be made if the full cost of the relevant research project is available, and available to be ringfenced. This prudent financial policy is appropriate given our size and specialism.

This policy meant that instead of being hit by a cash flow crisis in 2020, and the even worse possibility of not being able to pay for committed research grants, we were even able to announce new grant awards in 2020 and prepare to announce another grant call for 2021.

Plans for future periods

The Trust aims in 2021 to:

- Maintain excellence in family support, advocacy, information provision, and continue to make the introductions that families tell us are invaluable.
- Announce our 12th call for grants.
- Continue to work with key stakeholders in the neuromuscular disease community, and strategic rare disease organisations.
- Continue to work with the regulatory authorities on behalf of patients with myotubular and centronuclear myopathy – both the MHRA in the UK and the EMA in Europe.
- Plan ahead and prepare effectively for any future NICE review of treatments for myotubular and centronuclear myopathy, facilitating families' and patients' input.
- Partner with, and support TREAT-NMD on the long-term excellence and sustainability of the Myotubular and Centronuclear Myopathy Patient Registry.
- Continue to share information with, and promote collaboration between, other family and patient organisations, relevant scientific interest groups and research organisations.
- Continue to secure separate funding to cover the Trust's running costs.
- Maintain our 2020 support of fundraising events, despite the continued challenges brought about by the pandemic.

TRUSTEES' ANNUAL REPORT 31 December 2020

Reference and administrative details of the Charity, its Trustees and advisors

The following were Trustees of the Trust and held office during the above period:

Patricia Allen
Gary Browning
Greg Fowler
Andrew Lennox
Anne Lennox
James Rosling

Trustees are appointed by the board of trustees and serve for three years (five years for Anne Lennox) after which period they may put themselves forward for re-appointment. The trustees meet three times per annum.

Office

Myotubular Trust
- charity registration number 1137177
- company registration number 07260229

15a Barnard Road
London SW11 1QT

Bankers

CAF Bank Limited
Kings Hill
West Mailing
Kent
ME19 4JG

The Co-operative Bank
PO Box 250
Skelmersdale
WN8 6WT

Independent Examiner

Michael Stone MA ACA
Jamieson Stone LLP
Windsor House
40/41 Great Castle Street
London
W1W 8LU

Structure, Governance and Management

Constitution

The Myotubular Trust is an incorporated charity limited by guarantee and its governing document is the memorandum and articles of association dated 21 May 2010. The memorandum and articles of association has the same objects as that of the Trust Deed dated 26 January 2006 of the unincorporated charity. The Trust obtained charitable status under Section 4 of the Charities Act 1960 from the Charity Commission on 19 April 2006 under registration number 1113809 and following incorporation on the 20th May 2010 was registered with the Charity Commission with registration number 1137177, and with Companies House with company registration number 7260229.

Organisation and the Trustees

In selecting individuals for appointment, the trustees will have regard to the skills, knowledge and experience needed for the effective administration of the charity.

TRUSTEES' ANNUAL REPORT 31 December 2020

Trustees' responsibilities statement

The Trustees (who are also directors of The Myotubular Trust for the purposes of company law) are responsible for preparing the Trustees' Report and the financial statements in accordance with applicable law and United Kingdom Accounting Standards.

Company law in England and Wales requires the Trustees to prepare financial statements for each financial year in accordance with United Kingdom Generally Accepted Accounting Practice (United Kingdom Accounting Standards and applicable law). The financial statements are required by law to give a true and fair view of the state of affairs of the charity and of the income and expenditure of the charity for that period. In preparing these financial statements the trustees are required to:

- Select suitable accounting policies and then apply them consistently
- Observe the methods and principles of the Charities SORP
- Make judgments and estimates that are reasonable and prudent
- State whether applicable UK accounting standards have been followed and statements of recommended practice, subject to any departures disclosed and explained in the financial statements and
- Prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charity will continue to operate.

The trustees are responsible for keeping accounting records, which disclose with reasonable accuracy at any time the financial position of the charity and enable them to ensure that the financial statements comply with the Companies Act 2006. They are responsible for safeguarding the assets of the charity and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

Risk management

The trustees have examined the strategic, business and operational risks, which the charity faces and confirm that systems have been established to enable regular reports to be produced so that the necessary steps can be taken to lessen the risks.

INDEPENDENT EXAMINER'S REPORT FOR THE YEAR ENDED 31 DECEMBER 2020

Respective responsibilities of trustees and examiner

The trustees (who are also the directors of the company for the purpose of company law) are responsible for the preparation of the accounts. The charity's trustees consider that an audit is not required for this year under section 144 of the Charities Act 2011 (the Charities Act) and that an independent examination is needed.

Having been satisfied that the charity is not subject to audit under company law and is eligible for independent examination it is my responsibility to:

- examine the accounts under section 145 of the Charities Act,
- to follow the procedures laid down in the General Directions given by the Charity Commission (under section 145(5)(b) of the Charities Act, and
- to state whether particular matters have come to my attention.

Basis of independent examiner's statement

My examination was carried out in accordance with the General Directions given by the Charity Commission. An examination includes a review of the accounting records kept by the charity and a comparison of the accounts presented with those records. It also includes consideration of any unusual items or disclosures in the accounts, and the seeking of explanations from you as trustees concerning any such matters. The procedures undertaken do not provide all the evidence that would be required in an audit, and consequently, no opinion is given as to whether the accounts present a 'true and fair view' and the report is limited to those matters set out in the statement below.

Independent examiner's statement

In connection with my examination, no matter has come to my attention:

- 1) which gives me reasonable cause to believe that in, any material respect, the requirements:
 - to keep accounting records in accordance with section 130 of the Charities Act; and
 - to prepare accounts which accord with the accounting records and to comply with the accounting requirements of the Companies Act 2006 and with the methods and principles of the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2015) have not been met; or
- 2) to which, in my opinion, attention should be drawn in order to enable a proper understanding of the accounts to be reached

Michael Stone

Michael Stone MA ACA
Jamieson Stone LLP
Windsor House
40/41 Great Castle Street
London
W1W 8LU

20 August 2021

STATEMENT OF FINANCIAL ACTIVITIES FOR THE YEAR ENDED 31 DECEMBER 2020

	Unrestricted Funds £	Designated Funds £	Restricted Funds £	Total Funds 2020 £	Total Funds 2019 £
<u>INCOMING RESOURCES</u>					
Donations and grants	85,628	25,000	-	110,628	170,147
Fundraising activities	20,635	-	-	20,635	47,994
Interest received	1,602	-	-	1,602	1,468
	-----	-----	-----	-----	-----
Total incoming resources	107,865	25,000	-	132,865	219,609
	-----	-----	-----	-----	-----
<u>RESOURCES EXPENDED</u>					
Research	-	133,306	-	133,306	79,500
Fundraising costs	345	-	-	345	2,953
Staff costs	50,765	-	-	50,765	51,020
Training	-	-	-	-	81
Advocacy	-	12,187	-	12,187	13,891
Family Conference costs	-	-	-	-	-
Accountancy & payroll	110	-	-	110	280
Independent examiner	1,000	-	-	1,000	1,000
Legal & professional	-	-	-	-	-
Trustee's indemnity	966	-	-	966	865
Travel costs	216	-	-	216	1,403
Printing & stationery	72	-	-	72	337
Postage & telephone	56	-	-	56	140
Subscriptions	260	-	-	260	160
Web & IT costs	688	-	-	688	625
Bank charges	300	-	-	300	497
	-----	-----	-----	-----	-----
Total resources expended	54,778	145,493	-	200,271	152,752
	-----	-----	-----	-----	-----
Net incoming/(outgoing) resources	53,087	(120,493)	-	(67,406)	66,857
Transfers between funds	(51,194)	51,194	-	-	-
	-----	-----	-----	-----	-----
Net movement in funds	1,893	(69,299)	-	(67,406)	66,857
	-----	-----	-----	-----	-----
Total funds brought forward	4,069	358,340	-	362,409	295,552
	-----	-----	-----	-----	-----
Total funds carried forward	5,962	289,041	-	295,003	362,409
	-----	-----	-----	-----	-----

All gains and losses arising in the year are included within the statement of financial activities

The accompanying notes form part of these financial statements

Myotubular Trust

BALANCE SHEET AS AT 31 DECEMBER 2020

	£	2020 £	£	2019 £
CURRENT ASSETS				
Debtors and prepayments	26,275		1,561	
Cash at bank and in hand	270,455		364,280	
	-----		-----	
Total current assets	296,730		365,841	
	-----		-----	
CREDITORS				
Amounts falling due within one year	1,727		3,432	
	-----		-----	
Net current assets		295,003		362,409
		-----		-----
NET ASSETS		295,003		362,409
		-----		-----
FUNDS OF THE CHARITY				
Restricted funds		-		-
Unrestricted general funds		5,962		4,069
Unrestricted designated funds		289,041		358,340
		-----		-----
		295,003		362,409
		-----		-----

The company is entitled to exemption from audit under Section 477 of the Companies Act 2006 for the year ended 31 December 2020 and the members have not required the company to obtain an audit of its financial statements for the year ended 31 December 2020 in accordance with Section 476 of the Companies Act 2006.

The directors acknowledge their responsibilities for: (a) ensuring that the company keeps accounting records which comply with Sections 386 and 387 of the Companies Act 2006 and (b) preparing financial statements which give a true and fair view of the state of affairs of the company as at the end of each financial year and of its profit or loss for each financial year in accordance with the requirements of Sections 394 and 395 and which otherwise comply with the requirements of the Companies Act 2006 relating to financial statements, so far as applicable to the company.

The financial statements have been prepared in accordance with the provisions of Part 15 of the Companies Act 2006 relating to small companies.

The financial statements were approved by the trustees on ..20th August.2021..... and signed on their behalf:

Andrew Lennox

.....
Andrew Lennox
Chairman/Trustee

James Rosling

.....
James Rosling
Treasurer/Trustee

The accompanying notes form part of these financial statements

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2020

1. BASIS OF PREPARATION

The financial statements have been prepared on the accruals basis of historic cost in accordance with the Statement of Recommended Practice applicable to charities preparing their accounts in accordance with the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) (effective 1 January 2015) and the Companies Act 2006 and the Charities Act 2011.

2. ACCOUNTING POLICIES

Incoming Resources

Incoming resources are recognised when the charity becomes entitled to the resources, the trustees are virtually certain they will receive the resources, and the monetary value can be measured with sufficient reliability.

Where incoming resources have related expenditure (as with fundraising or contract income) the incoming resources and related expenditure are reported gross in the Statement of Financial Activities.

Grants and donations are recognised when the charity has unconditional entitlement to the resources.

Incoming resources from tax reclaims are recognised at the same time as the gift to which they relate.

Contractual income and performance related grants are recognized once the related goods or services have been delivered.

Investment income is included in the accounts when receivable.

Resources expended

Resources expended are recognised as soon as there is legal or constructive obligation committing the charity to pay out resources.

Resources expended include attributable VAT which cannot be recovered.

Funds

Restricted funds are funds to be used for specific purposes as declared by the donor.

Designated funds are monies set aside from general funds and designated for specific research awards by the trustees.

Unrestricted funds are donations and all other incoming resources without a specified purpose and which are available as general funds.

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED)

FOR THE YEAR ENDED 31 DECEMBER 2020

3. TAXATION

The Myotubular Trust is a registered charity and is not liable to Income Tax or Corporation Tax on income derived from its charitable activities.

4. RESOURCES EXPENDED

	2020 £	2019 £
Research	133,306	79,500
Independent examiner's remuneration	1,000	1,000
	-----	-----

The principal research grants awarded during the year were as follows:

	2020 £	2019 £
Sick Kids Canada - Dr Dowling	72,000	72,000
Sparks Charity GOSH	58,108	-
Taurus Tide	3,198	-
Newcastle University re Treat NMD	-	7,500
	-----	-----

5. DEBTORS AND PREPAYMENTS

	2020 £	2019 £
Gift Aid	133	175
Prepayments and accrued income	26,142	1,386
	-----	-----
	26,275	1,561
	-----	-----

6. CREDITORS FALLING DUE WITHIN ONE YEAR

	2020 £	2019 £
Accruals	1,727	3,432
	-----	-----

NOTES TO THE FINANCIAL STATEMENTS (CONTINUED) FOR THE YEAR ENDED 31 DECEMBER 2020

7. RELATED PARTY TRANSACTIONS

There were no related party transactions by the trustees for the year (2019: None).

One Trustee received remuneration of £20,000 during the year ending 31 December 2020 (2019: £20,000).

The trustee's remuneration and other administration costs are funded from unrestricted corporate and charitable donations, which were specifically raised for that purpose.