

Registered number: 10529899
Charity number: 1173589

PTEN RESEARCH FOUNDATION
FINANCIAL STATEMENTS
YEAR ENDED 31 MARCH 2023

PTEN RESEARCH FOUNDATION
(A company limited by guarantee)

CONTENTS

	Page
Reference and administrative details of the Charity, its Trustees and advisers	1
Trustees' report	2-11
Independent auditors' report on the financial statements	12-14
Statement of financial activities	15
Balance sheet	16
Statement of cash flows	17
Notes to the financial statements	18-33

PTEN RESEARCH FOUNDATION
A company limited by guarantee

REFERENCE AND ADMINISTRATIVE DETAILS OF THE CHARITY, ITS TRUSTEES AND ADVISERS
FOR THE YEAR ENDED 31 MARCH 2023

Trustees/Directors	Siriana Baldini Susannah Clark Renata Crome Robert Williams Riccardo Zacconi
Company Registered Number	10529899
Charity Registered Number	1173589
Registered Office	4 th Floor St James House Cheltenham GL50 3PR
Independent auditors	Crowe U.K. LLP 4 th Floor St James House Cheltenham GL50 3PR
Investment Manager	Brown Advisory 18 Hanover Square London, W1S 1JY
Bankers	Barclays Wealth Mayfair London W1K 1AF JP Morgan SE 6 Route de Treves L-2633 Senningerberg Luxembourg

PTEN RESEARCH FOUNDATION
(A company limited by guarantee)

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

The Trustees, who are also Directors for the purposes of Company Law, present their annual report together with the audited financial statements of the charity for the year 1st April 2022 to 31st March 2023. The Trustees confirm that the Annual Report and financial statements of the company comply with the current statutory requirements, the requirements of the company's governing document and the provisions of the Statement of Recommended Practice (SORP), 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).

Trustees

The trustees who served during the period were:

Siriana Baldini
Susannah Clark
Renata Crome
Robert Williams
Riccardo Zacconi

Riccardo Zacconi has signed the report on behalf of the Board of Trustees and the Directors.

Members

The company currently has a single member, Blue Compass PTC Limited, which has been in place since 16th December 2016.

Structure, governance and management

1. Name of the governing document and how the charity is constituted

The PTEN Research Foundation ('the Foundation' or 'PTEN Research') was established as a charity under English and Welsh law in 2017 (registered number 1173589). The Foundation is constituted under a Memorandum of Association and Articles of Association, dated 16th December 2016, which were revised by a special resolution of the Foundation's member on 18th July 2022 (the 'Revised Articles'). The Foundation's mission is to fund and facilitate research that will lead to better treatments and improved outcomes for PTEN hamartoma tumour syndrome ('PHTS').

2. Methods used to recruit and appoint new trustees

Under the Revised Articles, PTEN Research must have not less than three trustees and unless and until the Charity determines otherwise by ordinary resolution, the number of its trustees is not subject to a maximum limit.

The appointment, recruitment, and terms of office of trustees are determined by the governance needs of the Foundation to meet its mission. New trustees are recruited through relevant scientific, research or business networks. Active consideration is given to the diversity of the Board. Any person who is willing to act as a trustee and is permitted by law to do so, may be appointed by an ordinary resolution of the member. To date trustees have been appointed based on their skills and knowledge, and the contribution they can offer the Foundation.

3. The charity's organisational structure and how decisions are made

The organisational structure of the Foundation is as follows:

- **Board of Trustees:** the governing entity; the board ratifies policy and makes operational, funding and strategic decisions by majority vote.
- **Staff:** responsible for carrying out the day-to-day activities of the charity in accordance with its charitable objectives. They are supervised by the trustees and supported in their decision making through a Delegated Scheme of Authority.
- **Scientific Advisory Board (SAB):** responsible for providing the Foundation with non-binding scientific advice on its programmes and strategy.

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

At PTEN Research, decisions are made by the trustees or by delegation of authority to staff who manage the daily running of the Foundation. Under the Revised Articles, decisions of the Board must be supported by a majority of the trustees either in person or in writing. The trustees and member can exercise the powers of the charity as described in the published Revised Articles. As at 31st March 2023, and as at the date of this report, the Foundation's Board of Trustees included five individuals with knowledge in the fields of drug development, finance, communications, law and business development. The trustees meet at least four times a year.

The Foundation has a small team of staff who have the delegated authority to oversee the day-to-day running of the charity, ensuring that it adheres to its charitable objectives and mission.

At 31st March 2023, the Scientific Advisory Board (the 'SAB') comprised ten experts whose specialisms included: medicine and genetics, scientific research including specifically drug development, and clinical research. The SAB meets on average once a year to discuss the scientific progress of the Foundation. The SAB is also consulted during the year to advise on grants or to give input into scientific projects. SAB members have an advisory role and no decision-making authority.

4. Policies and procedures for induction and training of trustees

On appointment, new trustees sign a trustee declaration statement committing their time and expertise to the Foundation. After an initial meeting at which new trustees meet the Foundation's staff, they are introduced to the Foundation's grant making process, policies and procedures, and other relevant activities. New trustees are given access to the Foundation's governing documents, HR policies, financial information, annual reports and accounts, meeting materials and essential trustee guidance provided by the Charity Commission. In May and June 2022, Trustees were provided with two training modules commissioned from an external consultant, which covered trustees' duties and responsibilities as required by law and best practice.

5. Arrangements for setting pay and remuneration of key management personnel

Trustees are not remunerated for their work. Trustee expenses are reimbursed in line with Foundation policy. Pay and remuneration of key management staff is set by the trustees after a review of relevant market data. Key management staff comprise the Chief Executive, the Director of Translational Medicine and the Director of Finance and Business Operations. Staff pay and remuneration are reviewed annually.

6. The Charities (Protection and Social Investment) Act 2016

The Foundation is a larger charity as defined by S144(2) of the Charities Act 2011. As such, under The Charities (Protection and Social Investment) Act 2016, it must provide information and undertakings in respect of fund-raising activities carried out during the period under review in its trustees' report. During the year ended 31st March 2023, the Foundation did not engage a professional fundraiser or commercial participator or any other person to raise funds on its behalf; neither the Foundation nor anyone acting on its behalf was subject to an undertaking to be bound by any voluntary scheme for regulating fund-raising, or any voluntary standard of fund-raising; and no complaints were received by the Foundation or any person acting on its behalf about fund raising activities. The Foundation's website states that volunteers are not authorised to raise funds on its behalf, and that volunteers who choose to raise funds in aid of the Foundation are solely responsible for all aspects of those activities, for which the Foundation has no liability. The Foundation's website encourages 'in aid of' fundraisers to act within the law.

Objectives and Activities

1. Purposes of the charity and strategy

Under its governing documents, the Foundation's purposes are specifically restricted to: *"the protection and promotion of the health of individuals diagnosed with PTEN hamartoma tumour syndrome (PHTS) or other related conditions (by mechanism, clinical presentation or other factors) in particular by research into the nature, causes, diagnosis, prevention, treatment and cure of PHTS or other related conditions, including the development of findings of research into practical applications for the prevention, treatment and cure of PHTS or other related conditions, and in furtherance of that primary object, to increase awareness of PHTS or other related conditions and provide information and support as appropriate to affected individuals and families; and all purposes that are of public benefit and are exclusively charitable under the law of England and Wales."*

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

PHTS is a rare genetic disease caused by alteration (mutation) to the PTEN gene. These alterations may be inherited from the mother or father, or they may occur spontaneously during embryonic development. They result in a variety of symptoms and signs, including macrocephaly (enlarged head circumference), learning difficulties, autism spectrum disorder, vascular (blood vessel) anomalies, gastrointestinal polyps (growths in the gut), and hamartomas (benign lesions of the skin and other tissues). In addition, people with PHTS have a significantly increased lifetime risk of developing cancer, particularly cancers of the breast, thyroid, and endometrium (lining of the womb).

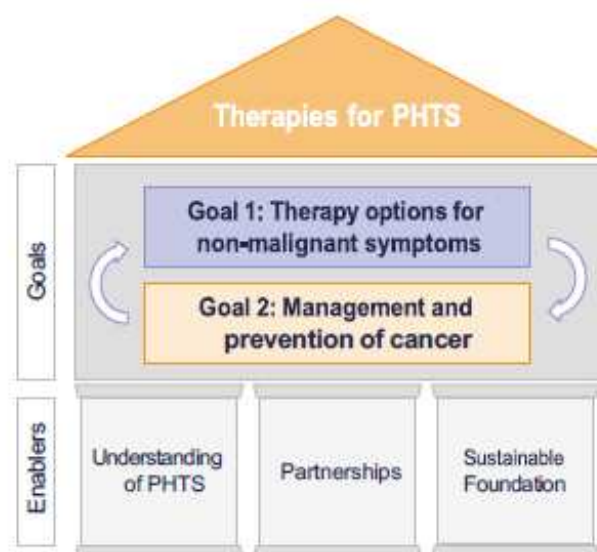
Due to its variable presentation, the true prevalence of PHTS in the general population is not known but is estimated to be about 1 in 200,000 [1]; however, more recent studies based on the prevalence of PTEN mutations in ASD suggest the prevalence of PHTS may be significantly higher. In a recent large study with sequencing data from 5,100 individuals with ASD, PTEN was one of the most common genes with ASD associated rare variants [2] and based on a meta-analysis of 9 studies [3] it has been estimated that 2% of individuals with ASD harbour a PTEN germline mutation [4].

There are currently no health-authority-approved treatments specific to PHTS, and clinical management of patients is largely focused on cancer surveillance and supportive care, which are associated with a high burden on healthcare systems. Consequently, there is a high unmet need for therapies to treat and, ultimately in the future, to potentially prevent the various symptoms associated with PHTS, as well as to improve the understanding of the syndrome to enable more accurate prognoses and improved management for diagnosed individuals. Developing therapies which mitigate the high burden on health systems is therefore for the wider public benefit.

The Foundation's strategy centres on the generation of preclinical and clinical evidence that will enable the Foundation, and others (both academic collaborators and industry), to develop treatment options for PHTS. We will continue to manage a portfolio of projects to support ongoing research efforts into PHTS and establishing new partnerships. At a cellular level, the genetic alterations to the PTEN gene result in PHTS cause dysregulation of the PI3K/AKT/mTOR pathway. This pathway has been the subject of extensive scientific study because it is often abnormal in acquired (sporadic) cancers that occur in the general population. As result, it may be possible to repurpose inhibitors of the PI3K/AKT/mTOR pathway that were originally developed to treat common cancers to treat individuals with PHTS.

The Foundation carries out its objects by implementing activities that support delivery of its strategy as depicted in Figure 1.

Figure 1: The Foundation's strategic goals & critical enabling activities



The central focus of our work is the development of therapy options for the non-malignant symptoms of PHTS that are clinically tractable and have a clear unmet need (Goal 1). In addition, the Foundation is increasingly focused on activities associated with PHTS and malignant disease (Goal 2). These include timely PHTS diagnosis to facilitate the initiation of cancer surveillance prior to a cancer diagnosis, as well as management of

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

malignant disease when this occurs. Whilst continuing to be a longer-term aspiration of the Foundation, cancer prevention strategies are highly challenging at present.

Activities that are integral to ensuring the success of therapy development efforts, but not strategic goals per se, are detailed as 'Enablers'. These encompass research efforts to improve understanding of both the biology of PTEN and PHTS, development of partnerships with key stakeholder groups, and development of a financially sustainable Foundation.

The work undertaken to fulfil the Foundation's objectives in the field of PHTS may have beneficial effects that extend well beyond PHTS. In particular, basic scientific and clinical research aimed at understanding the pathobiology of cancer in PHTS may improve the understanding of cancers more generally.

Similarly, work on vascular anomalies, soft tissue overgrowth and hamartomas in PHTS, has the potential to benefit patients with other genetic disorders which predispose to these manifestations, as well as patients with sporadic non-syndromic conditions.

Also, in the field of neuroscience, there are number of other neurodevelopmental conditions characterised by genetic alterations in cellular pathways that overlap with or are linked to, the PI3K/AKT/mTOR pathway. These include tuberous sclerosis complex (caused by alterations in the TSC1 and TSC2 genes), Phelan-McDermid syndrome (caused by SHANK3 gene alterations), Fragile X (alterations in FMRP gene) and Rett Syndrome (alterations in MeCP2 gene). Clinical and scientific knowledge gained in PHTS has the potential to support advancement in these related conditions and beyond, for example, in non-syndromic autism spectrum disorder.

Finally, PHTS is a rare disease and conducting trials in rare diseases brings particular challenges. Approaches taken by the Foundation may help others who face similar issues. For example, the development of new and more efficient trial designs and disease-specific trial endpoints, partnering with pharmaceutical and biotech companies and contract research organisations (as well as academic collaborators), and early engagement with regulatory agencies, may provide paradigms for other charitable organisations working in rare diseases. The Foundation's strategy, future plans, and budgets are annually reviewed and agreed by the trustees.

2. Activities undertaken in the year

The total expenditure for the year ending 31st March 2023 was £4,104,540. This expenditure supported implementation of the Foundation's objects as defined in the Articles of Association and further detailed in the Foundation's strategy document. Expenditure was subject to initial approval by the Foundation's board and subject to ongoing periodic review.

The total income received for the period ending 31st March 2023 was £646,935. This income was a result of the following activities:

- Restricted donations received: £911, as a result of restricted donations given to the Foundation for the purposes of funding medical research projects.
- Unrestricted donations received: £nil.
- Investment income received: £646,024.

3. Criteria used to assess the success of the reporting period

The Trustees meet at least once a quarter. A standing item of the board meetings is to assess the progress of the Foundation against its agreed annual goals, project progress as detailed in the Foundation's dashboard and strategic objectives.

4. Review of significant activities undertaken to further charitable objectives for the public benefit

Statement of Confirmation

The Trustees confirm that they have given due consideration to the Charity Commission's published guidance on the public benefit requirement under Charities Act 2011. They believe the development of therapy options for PHTS patients (the Foundation's primary object) will alleviate significant unmet medical needs of PHTS patients as well as the high burden on healthcare systems associated with the condition, as is further explained in the overview below.

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

Overview: activities undertaken to further charitable objectives for the public benefit

The Foundation's principal charitable objective is to protect and promote the health of individuals diagnosed with PTEN hamartoma tumour syndrome (PHTS) or other related conditions.

There were 20 active projects at the year-end, of which 17 were with academic collaborators and the rest with commercial partners. Several projects were in active development with 16 having been previously completed. Since its inception, the work of the Foundation has been acknowledged in 43 peer reviewed academic research papers published in scientific journals. (A full listing of publications may be found at <https://www.ptenresearch.org/for-researchers-and-professionals/projects-and-publications/publications/>) These activities have materially increased scientific knowledge associated with PHTS.

Significant progress was made on several key scientific projects:

- Following positive feedback from the inaugural meeting in 2022, a second Foundation-led scientific meeting was held for key funded researchers and collaborators in the field in order to share and present summaries of their current research in order to promote collaboration amongst the PHTS research community. Based on the positive experience of the past two years, it is planned to make this an annual event.
- Following a joint application between the Foundation and academic investigators (Prof. Charis Eng and David Flannery M.D., from Cleveland Clinic Genomic Medicine Institute, and Prof. Marc Tischkowitz, from the Department of Medical Genetics at Cambridge University), appropriate and relevant codes for PHTS were incorporated into ICD-10-CM by the US Centers for Disease Control and Prevention (CDC) and ICD 11 by the World Organisation (WHO) respectively. The availability of these codes is hoped to support refinement of the estimated prevalence of PHTS and support identification of trial subjects for future clinical studies.
- Data from the Foundation funded trial randomized controlled trial of everolimus for neurocognitive symptoms in PTEN hamartoma tumour syndrome (NCT02991807) were published in Human Molecular Genetics.
- A Foundation-funded grant led by Radboud University in the Netherlands focusing on retrospective analysis of data from a European cohort of PHTS patients to refine the risk of cancer, was successfully completed and two manuscripts were published. The first published in the Journal of the National Cancer Institute (JNCI) refined estimates of PHTS cancer risk based on large retrospectively collected European cohort which was corrected to ascertainment biases. The second published in the European Journal of Medical Genetics focused on genotype-phenotype association in PHTS. A second grant with the same institution focused on PHTS cancer risk and prognosis is approaching completion.
- The Foundation launched a formal targeted call with the goal of providing grants to elucidate improved understanding of the role of non-canonical functions of PTEN in PHTS. Sixteen full applications were received and underwent external peer review with two ultimately having been selected for funding:
 - A study to investigate how PHTS-associated missense variants impact PTEN function and contribute to PHTS pathophysiology and distinct disease states, facilitating the identification of targets for development of novel treatments (University of British Columbia, Canada).
 - A study of non-canonical functions of PTEN (mTOR-independent mechanism) and their impact on neuronal activity in pre-clinical models of PTEN loss in the brain, with the aim of developing novel and more efficient drug treatments to cognitive deficits in PHTS patients (Geisel School of Medicine, Dartmouth Collected USA).
- Collaborations with two Contract Research Organisations (CROs) have made significant progress, enabling the evaluation of a large panel of approved and clinical phase small molecule inhibitors of the PI3K pathway. In addition to sourcing inhibitors from commercial sources we have also tested a number of compounds provided by pharma and biotech organisations.
 - In collaboration with Evotec we have established cell based models to assess the activity of compounds in assays reflecting aberrant neuronal cell behaviour arising from PTEN loss.
 - In collaboration with Charles River Laboratories, the same panel of compounds are currently undergoing assessment in cellular assays of aberrant vascular and adipose cell growth arising from PTEN loss.
 - In addition to cellular models of PTEN loss, we have made progress to develop in vivo models

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

of PHTS through genetically engineering PTEN loss in the CNS and in the skin. During 2024, these models will be available to test compounds prioritised by the in vitro screening.

- The vascular biology group at the Josep Carreras Leukaemia Research Institute (Barcelona) have continued to develop additional models of PHTS vascular malformations. The collaboration has evaluated a small number of clinical stage inhibitors of the PI3K pathway and continues to investigate the mechanism of PTEN loss and its impact on vascular cell biology.
- An ongoing collaboration with University College London has evaluated the activity of several clinical stage compounds that selectively target different components of the PI3K signalling pathway. Based on a mouse model that mimics human PTEN loss, the studies are an extension of the previous evaluation of rapamycin and aim to provide evidence to support additional clinical candidates for PHTS.

Governance:

In the year ending 31st March 2023, the Foundation continued to strengthen its governance. A review of the Foundation's constitution by a firm of charity-specialist solicitors led to revisions to its articles of association which were adopted by special resolution by the Foundation's member on 18th July 2022. In addition, a new Trustee Policy of 4th November 2022 codified committees of the Board into the governance structure.

Processes for regular reporting and risk escalation to ensure transparent and informed decision-making continue to be used to guide the Foundation's grants and work.

Strategy:

The Foundation's strategy is continually refined and incrementally updated on the basis of emerging data. In addition, the team recently developed a Five Year/Medium Term Plan highlighting key planned activities and goals for the coming years. A longer-term financial plan of activities to deliver the strategy is proactively maintained and costed for the period to March 2030, incorporating expenditure forecasts that are updated and revised on a six-monthly basis.

Staff:

As a result of the pandemic, the Foundation's staff were required to transition to home-based working. Despite the restrictions being lifted, the Trustees and senior staff team have elected to retain this virtual working model as it not only reduces office rental costs but also allows access to a broader talent pool of staff free from geographical restrictions. Mindful of some of the potential downsides associated with permanent virtual working the team have instigated regular face to team meetings and worked with an external facilitator to provide training and support to the team on leadership, engagement, roles and responsibilities and maximizing productivity in a virtual environment.

Policies, Guidance Documents and Process:

The Foundation continues to maintain and develop policies and processes for HR, operations, financial awards and fundraising, as required.

Clinical Development Working Groups (CDWGs):

These are multidisciplinary groups of international PHTS thought leaders supporting the Foundation with outputs envisaged to play a key role in shaping and optimising the design of future prospective PHTS clinical, natural history and translational medicine studies with a goal of improving patient care more broadly. The continued development of the CDWGs over the last year has provided significant value to the Foundation.

Patient engagement:

The Foundation maintains regular interactions with patient advocacy groups. These include both dedicated meetings, a quarterly newsletter drafted in lay language and patient group presentations highlighting key Foundation activities on a periodic basis.

Recognising the importance of soliciting important feedback from PHTS patients and their families as the community that the Foundation seeks to support, our research grant application process has been revised to ensure applicants not only provide details of how the proposed project will benefit the wider PHTS community

PTEN RESEARCH FOUNDATION
(A company limited by guarantee)

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

of individuals with PHTS and their caregivers and families but also detail their interactions with PHTS patient organisations or other patient representatives in developing the application and how the feedback received has influenced the scope of the application. As noted in previous years the Foundation cannot offer specific advice to individual patients.

Analysis of publicly available scientific and medical literature:

Desk research continues to be undertaken on publications relating to the natural history and the mechanism of disease of PHTS. Trustees and the staff team regularly review these developments to ensure the Foundation's activities remain relevant and robust.

Policy on grant and non-grant funding:

The Foundation provides grants in line with its strategic goals and mission.

The Foundation funds research projects that can translate into better treatments for PHTS patients. These include interventional clinical trials, natural history studies and patient registries, preclinical/translational research projects and, where appropriate, basic research projects.

Funding is primarily provided through two mechanisms:

- Targeted calls
- Innovation Awards

Discussions arising from the Clinical Development Working Groups have also led to several grant applications.

Grants are awarded to Principal Investigators who have qualified with an MD or PhD and who have an established research programme in a recognised academic or clinical research institution. Eligibility is not restricted to any specific geography.

Funding is intended to support all essential costs relating to a project, including staff, consumables, equipment, travel and publication costs. The Foundation's policy is to pay only those costs that are directly attributable to the activities of the grant.

Applications undergo a scientific, strategic, and programmatic assessment by the Foundation's internal research team. Successful applications at this stage are then generally submitted for external peer review by at least two independent subject matter experts. The peer-reviewed applications are then subject to review by the Scientific Advisory Board (SAB) prior to a final approval by trustees.

In addition to grants, the Foundation commissions work with industry partners including contract research organisations (CROs) in the pursuit of its mission. This contracted work undergoes a scientific, strategic and programmatic assessment by the Foundation's internal research team before work commences.

Fundraising:

The Foundation received £911 in donations (all restricted).

1. Use of volunteers

At present the Foundation does not utilise volunteer staff. As previously noted, trustees are engaged on a voluntary basis.

2. Fundraising activities

The Foundation is primarily funded through one-off donations and income from its investments. In addition, the Foundation has recently prepared a fund-raising strategy paper and has retained professional charity fund raising consultancy with a view to more formally assessing further fundraising activities in the future.

When negotiating legal agreements, including grant terms and conditions, the Foundation actively seeks to equitably share with its academic and commercial partners any potential arising intellectual property ownership, commercialisation rights and/or royalties relative to the proportion of the total costs funded by the Foundation.

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

Further, by highlighting the unmet medical need of PHTS to pharmaceutical and biotech organisations coupled with potential regulatory incentives associated with both paediatric and rare disease drug development applicable to PHTS, we hope that such organisations may not only provide direct financial support to the charity to access preclinical models developed by the Foundation but also may independently support PHTS drug development.

Risk management:

We recognise the inherent risks associated with the development of therapy options for a rare disease such as PHTS given the complexity of the syndrome and low number of patients worldwide. In common with other organizations supporting drug development and life sciences, not all projects supported by the Foundation can be expected to have a positive outcome. However, negative outcomes can often inform our future strategy and provide valuable scientific data and learnings. Potential risks include, but are not limited to, the potential failure of preclinical studies and/or clinical trials to meet safety or efficacy endpoint criteria, the potential unwillingness of industrial partners to support PHTS development, and the challenges of meeting the requirements of global Health Authorities to ensure drug approvals in the rare disease setting.

In some cases, we will actively choose to undertake multiple activities in parallel to enhance the probability that we will ultimately fulfil our mission, as well as gate certain future activities on the read-out of predecessors. To ensure good stewardship of charitable funds the Foundation actively seeks the guidance of key opinion leaders in the PHTS field worldwide both via the SAB and the CDWGs. Further, grants continue to be independently peer reviewed, follow robust contracting procedures and are subject to active monitoring and evaluation by Foundation staff.

Whilst the immediate direct impact of the COVID-19 pandemic has largely passed, healthcare systems globally continue to report pressures in relation to catching up with clinical case backlogs and staffing issues resulting from the previous disruption. This has led to ongoing delays of certain clinical projects. We continue to monitor the situation closely in the context of ongoing and future planned activities with our key partners.

To enable active portfolio and risk management, the Foundation uses a project dashboard with visualisations of our portfolio of projects by phase, associated project risks, and financial analyses. It is acknowledged that, in the future, a more active approach to portfolio management will be needed, based not only on emerging data and which projects are most likely to lead to a future treatment for PHTS patients but which also considers the need for the Foundation to operate within its available funds. We utilise standard industry attrition rates of projects by phase to inform decision making and portfolio management and undertake a 6-monthly review of forecast of expected annual expenditure for the following 6-7-year period, in both fully loaded and attrition-adjusted models.

Potential risks also arise in relation to our finances. Though we have a generous endowment, our resources are finite. The Foundation has a bond portfolio whose constituents are held to maturity and a growth investment portfolio which together might reasonably be expected to cover expenditure to March 2030. If inflationary conditions persist, however, the bond portfolio may fall short of the outgoings it is designed to fund. Moreover, the value of the growth portfolio depends on financial markets which have suffered from the war in Ukraine, inflation, rising interest rates and fears of recession.

The following other risks have been identified in our operational risk register and remedial action taken.

- Following a Charity Commission alert issued on behalf of the National Cyber Security Centre, we revised our IT policy and instituted staff training on best practice in the first quarter of 2022, and further remedial action is in development.
- Conscious of the need for good internal controls, we strive to remedy weaknesses identified by our auditors, and now maintain our own investment records following an audit recommendation in 2021.
- Given that staff work from home, and the risk that this may detract from staff's ability to work as a cohesive team, we have supplemented virtual staff interaction with monthly physical meetings, and organisational training provided by an independent consultant.
- Finally, to ensure good governance, we commissioned a governance review from an independent consultant, following which our trustee policy was updated and the same consultant has provided training to our trustees.

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

Financial Review:

1. Review of the charity's financial position as at the end of the reporting period

At the end of the reporting period the Foundation holds no restricted funds.

The Charity holds general funds of £26,399,346 to be used for direct and support costs over the period to 31st March 2030.

2. Investment management

Following a formal review and retendering of the investment management function with the goal of ensuring appropriate liquidity to meet the Foundation's short-term liabilities whilst also maximising the opportunity for investment growth, Brown Advisory were engaged as the Foundation's new and exclusive investment manager in April 2021.

Brown have created a portfolio of bonds to be held to maturity a growth investment portfolio which together might reasonably be expected to cover forecast spend to March 2030. Of the securities in these portfolios, at least 85% must be realizable into cash within 5 business days; and up to a maximum 15% within 45 business days.

3. Reserves Policy and Going Concern

The Foundation does not implement a reserves policy.

All restricted and unrestricted donations received to date have been accounted for in the Foundation's accountancy software and are clearly split with respect to purpose and use.

With due regard to the Foundation's finances and projected expenditure, the trustees remain satisfied that it has sufficient resources to continue as a going concern for at least 12 months after the approval of the financial statements to which this report relates.

4. Plans for Future Periods

In the coming year, the Foundation's existing granted and industry-based collaborations will continue to progress.

The Foundation will continue to forge links with members of the professional and patient communities, with the aim of facilitating future collaborative working. To this end, the Foundation intends to hold further scientific meetings with its funded researchers and collaborators to enhance sharing of knowledge and promote synergy. Foundation staff will continue to participate in other events, meetings and patient days, where appropriate.

In the immediate term, we plan to sign grant award letters with two applicants who responded to our targeted call in 2021 for grants specifically to elucidate and support improved understanding of role of non-canonical functions of PTEN in PHTS.

Trustees' Responsibilities Statement

The Trustees (who include all the directors of PTEN Research Foundation 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 (United Kingdom Generally Accepted Accounting Practice).

Company law requires the Trustees to prepare financial statements for each financial year. Under company law the Trustees must not approve the financial statements unless they are satisfied that they give a true and fair view of the state of affairs of the charitable company and of the incoming resources and application of resources, including the income and expenditure, of the charitable company 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 in the Charities SORP and FRS 102;

PTEN RESEARCH FOUNDATION
(A company limited by guarantee)

TRUSTEES' REPORT FOR THE YEAR ENDED 31 MARCH 2023

- make judgments and accounting estimates that are reasonable and prudent;
- prepare the financial statements on the going concern basis unless it is inappropriate to presume that the charitable company will continue in operation.

The Trustees are responsible for keeping adequate accounting records that are sufficient to show and explain the charitable company's transactions and disclose with reasonable accuracy at any time the financial position of the charitable company and enable them to ensure that the financial statements comply with the Companies Act 2006. They are also responsible for safeguarding the assets of the charitable company and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

Disclosure of information to Auditors

Each of the persons who are Trustees at the time when this Trustees' Report is approved has confirmed that:

- so far as that Trustee is aware, there is no relevant audit information of which the charitable company's auditors are unaware, and
- that Trustee has taken all the steps that ought to have been taken as a Trustee in order to be aware of any relevant audit information and to establish that the charitable company's auditors are aware of that information.

In preparing this report, the Trustees have taken advantage of the small companies' exemption provided by section 415A of the Companies Act 2006.

This report was approved by the Trustees, on 27th November, 2023 and signed on their behalf by:



Riccardo Zacconi
Trustee, PTEN Research Foundation

References

- [1] M. R. Nelen *et al.*, "Novel PTEN mutations in patients with Cowden disease: absence of clear genotype–phenotype correlations," *European Journal of Human Genetics*, vol. 7, pp. 267–273, 1999, [Online]. Available: <http://www.stockton-press.co.uk/ejhg>
- [2] B. Trost *et al.*, "Genomic architecture of autism from comprehensive whole-genome sequence annotation," *Cell*, vol. 185, no. 23, pp. 4409–4427.e18, Nov. 2022, doi: 10.1016/j.cell.2022.10.009.
- [3] A. K. Tilot, T. W. Frazier, and C. Eng, "Balancing Proliferation and Connectivity in PTEN-associated Autism Spectrum Disorder," *Neurotherapeutics*, vol. 12, no. 3. Springer New York LLC, pp. 609–619, Jul. 22, 2015. doi: 10.1007/s13311-015-0356-8.
- [4] T. W. Frazier, "Autism Spectrum Disorder Associated with Germline Heterozygous *PTEN* Mutations," *Cold Spring Harb Perspect Med*, vol. 9, no. 10, p. a037002, Oct. 2019, doi: 10.1101/cshperspect.a037002.

INDEPENDENT AUDITORS' REPORT TO THE MEMBERS OF PTEN RESEARCH FOUNDATION

FOR THE YEAR ENDED 31 MARCH 2023

Opinion

We have audited the financial statements of PTEN Research Foundation ('the charitable company') for the year ended 31 March 2023 which comprise the Statement of Financial Activities, the Balance Sheet, the Statement of Cash Flows and notes to the financial statements, including significant accounting policies. The financial reporting framework that has been applied in their preparation is applicable law and United Kingdom Accounting Standards, including Financial Reporting Standard 102 The Financial Reporting Standard applicable in the UK and Republic of Ireland (United Kingdom Generally Accepted Accounting Practice).

In our opinion the financial statements:

- give a true and fair view of the state of the charitable company's affairs as at 31 March 2023 and of its income and expenditure, for the year then ended;
- have been properly prepared in accordance with United Kingdom Generally Accepted Accounting Practice; and
- have been prepared in accordance with the requirements of the Companies Act 2006.

Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) (ISAs (UK)) and applicable law. Our responsibilities under those standards are further described in the Auditor's responsibilities for the audit of the financial statements section of our report. We are independent of the charitable company in accordance with the ethical requirements that are relevant to our audit of the financial statements in the UK, including the FRC's Ethical Standard, and we have fulfilled our other ethical responsibilities in accordance with these requirements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Conclusions relating to going concern

In auditing the financial statements, we have concluded that the trustee's use of the going concern basis of accounting in the preparation of the financial statements is appropriate.

Based on the work we have performed, we have not identified any material uncertainties relating to events or conditions that, individually or collectively, may cast significant doubt on the charitable company's ability to continue as a going concern for a period of at least twelve months from when the financial statements are authorised for issue.

Our responsibilities and the responsibilities of the trustees with respect to going concern are described in the relevant sections of this report.

Other information

The trustees are responsible for the other information contained within the annual report. The other information comprises the information included in the annual report, other than the financial statements and our auditor's report thereon. Our opinion on the financial statements does not cover the other information and, except to the extent otherwise explicitly stated in our report, we do not express any form of assurance conclusion thereon. Our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the financial statements, or our knowledge obtained in the audit or otherwise appears to be materially misstated. If we identify such material inconsistencies or apparent material misstatements, we are required to determine whether this gives rise to a material misstatement in the financial statements themselves. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report in this regard.

INDEPENDENT AUDITORS' REPORT TO THE MEMBERS OF PTEN RESEARCH FOUNDATION

FOR THE YEAR ENDED 31 MARCH 2023

Opinions on other matters prescribed by the Companies Act 2006

In our opinion based on the work undertaken in the course of our audit

- the information given in the trustees' report, which includes the directors' report prepared for the purposes of company law, for the financial year for which the financial statements are prepared is consistent with the financial statements; and
- the directors' report included within the trustees' report have been prepared in accordance with applicable legal requirements.

Matters on which we are required to report by exception

In light of the knowledge and understanding of the charitable company and their environment obtained in the course of the audit, we have not identified material misstatements in the directors' report included within the trustees' report.

We have nothing to report in respect of the following matters in relation to which the Companies Act 2006 requires us to report to you if, in our opinion:

- adequate and proper accounting records have not been kept; or
- the financial statements are not in agreement with the accounting records and returns; or
- certain disclosures of trustees' remuneration specified by law are not made; or
- we have not received all the information and explanations we require for our audit.

Responsibilities of trustees

As explained more fully in the trustees' responsibilities statement set out on page 10-11, the trustees (who are also the directors of the charitable company for the purposes of company law) are responsible for the preparation of the financial statements and for being satisfied that they give a true and fair view, and for such internal control as the trustees determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, the trustees are responsible for assessing the charitable company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the trustees either intend to liquidate the charitable company or to cease operations, or have no realistic alternative but to do so.

Auditor's responsibilities for the audit of the financial statements

Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance but is not a guarantee that an audit conducted in accordance with ISAs (UK) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

Details of the extent to which the audit was considered capable of detecting irregularities, including fraud and non-compliance with laws and regulations are set out below.

A further description of our responsibilities for the audit of the financial statements is located on the Financial Reporting Council's website at: www.frc.org.uk/auditorsresponsibilities. This description forms part of our auditor's report.

INDEPENDENT AUDITORS' REPORT TO THE MEMBERS OF PTEN RESEARCH FOUNDATION

FOR THE YEAR ENDED 31 MARCH 2023

Extent to which the audit was considered capable of detecting irregularities, including fraud

Irregularities, including fraud, are instances of non-compliance with laws and regulations. We identified and assessed the risks of material misstatement of the financial statements from irregularities, whether due to fraud or error, and discussed these between our audit team members. We then designed and performed audit procedures responsive to those risks, including obtaining audit evidence sufficient and appropriate to provide a basis for our opinion.

We obtained an understanding of the legal and regulatory frameworks within which the charitable company operates, focusing on those laws and regulations that have a direct effect on the determination of material amounts and disclosures in the financial statements. The laws and regulations we considered in this context were the Companies Act 2006, together with the Charities SORP (FRS102) 2019. We assessed the required compliance with these laws and regulations as part of our audit procedures on the related financial statement items.

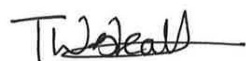
In addition, we considered provisions of other laws and regulations that do not have a direct effect on the financial statements but compliance with which might be fundamental to the charitable company's ability to operate or to avoid a material penalty. We also considered the opportunities and incentives that may exist within the charitable company for fraud.

Auditing standards limit the required audit procedures to identify non-compliance with these laws and regulations to enquiry of the Trustees and other management and inspection of regulatory and legal correspondence, if any. We identified the greatest risk of material impact on the financial statements from irregularities, including fraud, to be within the override of controls by management. Our audit procedures to respond to these risks included enquiries of management, and the Audit Committee about their own identification and assessment of the risks of irregularities, sample testing on the posting of journals, reviewing accounting estimates for biases, reviewing regulatory correspondence with the Charity Commission and reading minutes of meetings of those charged with governance.

Owing to the inherent limitations of an audit, there is an unavoidable risk that we may not have detected some material misstatements in the financial statements, even though we have properly planned and performed our audit in accordance with auditing standards. For example, the further removed non-compliance with laws and regulations (irregularities) is from the events and transactions reflected in the financial statements, the less likely the inherently limited procedures required by auditing standards would identify it. In addition, as with any audit, there remained a higher risk of non-detection of irregularities, as these may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal controls. We are not responsible for preventing non-compliance and cannot be expected to detect non-compliance with all laws and regulations.

Use of our report

This report is made solely to the charitable company's members, as a body, in accordance with Chapter 3 of Part 16 of the Companies Act 2006. Our audit work has been undertaken so that we might state to the charitable company's members those matters we are required to state to them in an auditor's report and for no other purpose. To the fullest extent permitted by law, we do not accept or assume responsibility to anyone other than the charitable company and the charitable company's members as a body, for our audit work, for this report, or for the opinions we have formed.



Tara Westcott

Senior Statutory Auditor

For and on behalf of: Crowe U.K. LLP, Statutory Auditor

4th Floor St James House, St James' Square, Cheltenham. GL50 3PR

Date: **28 November 2023**

PTEN RESEARCH FOUNDATION
(A company limited by guarantee)

STATEMENT OF FINANCIAL ACTIVITIES INCORPORATING INCOME AND EXPENDITURE ACCOUNT
FOR THE YEAR ENDED 31 MARCH 2023

	Note	Unrestricted Funds 2023 £	Restricted funds 2023 £	Total funds 2023 £	Total funds 2022 £
Income from:					
Donations	2		911	911	3,361
Investments	3	646,024		646,024	921,274
Total income		646,024	911	646,935	924,635
Expenditure on:					
Raising funds		97,085		97,085	98,903
Charitable activities:	4,5				
Direct costs		3,792,738	911	3,793,649	3,461,644
Support costs		213,806		213,806	142,232
Total expenditure		4,103,629	911	4,104,540	3,702,779
Net expenditure before net (losses) on investments		(3,457,605)		(3,457,605)	(2,778,144)
Net (losses)/gains on investments		(1,217,732)		(1,217,732)	(1,905,871)
Foreign exchange gains/(losses) on investments		924,425		924,425	621,965
Net movement in funds		(3,750,912)		(3,750,912)	(4,062,050)
Reconciliation of funds:					
Total funds brought forward		30,150,258		30,150,258	34,212,308
Net movement in funds		(3,750,912)		(3,750,912)	(4,062,050)
Total funds carried forward		26,399,346		26,399,346	30,150,258

The notes on pages 18 to 33 form part of these financial statements.

BALANCE SHEET

AS AT 31 MARCH 2023

	Note	2023 £	2022 £
Fixed assets			
Tangible assets	9	3,276	4,092
Investments	10	<u>20,052,722</u>	<u>21,817,348</u>
		20,055,998	21,821,440
Current assets			
Debtors	11	4,730	4,592
Investments	12	3,745,907	6,223,219
Cash at bank and in hand		<u>3,374,828</u>	<u>2,397,117</u>
		7,125,465	8,624,928
Creditors: amounts falling due within one year	13	<u>(782,117)</u>	<u>(296,110)</u>
Net current assets		<u>6,343,348</u>	<u>8,328,818</u>
Net assets		<u>26,399,346</u>	<u>30,150,258</u>
Charity funds			
Restricted funds	15	-	-
Unrestricted funds	15	<u>26,399,346</u>	<u>30,150,258</u>
Total funds		<u>26,399,346</u>	<u>30,150,258</u>

The financial statements were approved and authorised for issue by the Trustees and signed on their behalf by



Riccardo Zacconi

Trustee

Date: 27 November 2023

The notes on pages 18 to 33 form part of these financial statements.

STATEMENT OF CASH FLOWS

FOR THE YEAR ENDED 31 MARCH 2023

		2023	2022
	Note	£	£
Cash flows from operating activities			
Net cash provided by operating activities	17	<u>(3,615,695)</u>	<u>(4,003,589)</u>
Cash flows from investing activities			
Purchase of tangible fixed assets		(1,249)	(5,208)
Proceeds from sale of investments		9,743,034	10,610,372
Purchase of investments		(5,691,644)	(15,535,585)
Investment income		646,024	921,274
Transfer to investments from cash		<u>61,405</u>	<u>(167,577)</u>
Net cash provided by/(used in) investing activities		<u>4,757,570</u>	<u>(4,176,724)</u>
Change in cash and cash equivalents in the year		1,141,875	(8,180,313)
Cash and cash equivalents at the beginning of the year		2,397,117	10,562,584
Cash and cash equivalents due to exchange rate movements		<u>(164,164)</u>	<u>14,846</u>
Cash and cash equivalents at the end of the year		<u><u>3,374,828</u></u>	<u><u>2,397,117</u></u>

The notes on pages 18 to 33 form part of these financial statements

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

1. Accounting policies

General information

PTEN Research Foundation is a charitable company limited by guarantee incorporated in England on 16 December 2016 and registered with the Charity Commission on 27 June 2017. Its registered office address is 4th Floor, St James House, St James Square, Cheltenham GL50 3PR.

1.1 Basis of preparation of financial statements

The financial statements have been prepared in accordance with Accounting and Reporting by Charities: 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) - (Charities SORP (FRS 102)), the Financial Reporting Standard applicable in the UK and Republic of Ireland (FRS 102) and the Companies Act 2006.

PTEN Research Foundation meets the definition of a public benefit entity under FRS 102. Assets and liabilities are initially recognised at historical cost or transaction value unless otherwise stated in the relevant accounting policy. The accounts are prepared on the basis that the Charity is a going concern.

The accounts have been prepared in GBP sterling as this is the operating currency of the charity.

1.2 Company status

The sole member of the charity is Blue Compass PTC. In the event of the company being wound up, the liability in respect to the guarantee is limited to £1 per member of the charity.

1.3 Income

All income is recognised once the charity has entitlement to the income, it is probable that the income will be received, and the amount of income receivable can be measured reliably.

Donations are recognised in the period in which they are pledged.

Gifts of investments are measured at fair value and are recognised on the balance sheet with a corresponding amount being recognised in income.

1.4 Interest receivable

Interest on funds held on deposit is included when receivable and the amount can be measured reliably by the charity; this is normally upon notification of the interest paid or payable by the Bank.

1.5 Expenditure

Expenditure is recognised once there is a legal or constructive obligation to transfer economic benefit to a third party, it is probable that a transfer of economic benefits will be required in settlement and the amount of the obligation can be measured reliably. Expenditure is classified by activity. The costs of each activity are made up of the total of direct costs and shared costs, including support costs involved in undertaking each activity. Direct costs attributable to a single activity are allocated directly to that activity. Shared costs which contribute to more than one activity and support costs which are not attributable to a single activity are apportioned between those activities on a basis consistent with the use of resources. Central staff costs are allocated on the basis of time spent, and depreciation charges allocated on the portion of the asset's use.

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

1. Accounting policies (continued)

Charitable activities are costs incurred on the charity's operations, including support costs and costs relating to the governance of the charity apportioned to charitable activities.

Grants payable are charged in the year when the offer is made except in those cases where the offer is conditional, such grants being recognised as expenditure when the conditions attaching are fulfilled. Grants offered subject to conditions which have not been met at the year-end are noted as a commitment, but not accrued as expenditure. Support costs are those costs incurred directly in support of expenditure on the objects of the charity and include governance costs. All expenditure is inclusive of irrecoverable VAT. Accounting policies are supplemented by estimation techniques where judgement is required in measuring the value of income and expenditure.

Termination payments are recognised when the commitment is made to terminate employment.

1.6 Tangible fixed assets and depreciation

Tangible fixed assets are carried at cost, net of depreciation and any provision for impairment. Depreciation is provided at rates calculated to write off the cost of fixed assets, less their estimated residual value, over their expected useful lives on the following bases:

Computer equipment - 33% straight line

1.7 Investments

Current and fixed asset investments are a form of financial instrument and are initially recognised at their transaction cost and subsequently measured at fair value at the Balance Sheet date, unless fair value cannot be measured reliably in which case it is measured at cost less impairment. Investment gains and losses, whether realised or unrealised, are combined and shown in the heading 'Gains/(losses) on investments' in the Statement of Financial Activities incorporating Income and Expenditure Account.

Fixed asset investments are those investments held for the generation of investment income, investment potential or both and have a maturity of at least one year from the balance sheet date.

Current asset investments are those investments held for investment purposes rather than to meet short term cash commitments as they fall due. Current asset investments are expected to be realised within 12 months of the reporting date and include cash on deposit and cash equivalents with a maturity of less than one year.

1.8 Debtors

Trade and other debtors are recognised at the settlement amount after any trade discount offered. Prepayments are valued at the amount prepaid net of any trade discounts due.

1.9 Cash at bank and in hand

Cash at bank and in hand includes cash and short term highly liquid investments held to meet short term cash commitments as they fall due rather than for investment potential. Cash and short term highly liquid investments have a short maturity of three months or less from the date of acquisition or opening of the deposit or similar account.

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

1. Accounting policies (continued)

1.10 Liabilities and provisions

Liabilities are recognised when there is an obligation at the Balance Sheet date as a result of a past event, it is probable that a transfer of economic benefit will be required in settlement, and the amount of the settlement can be estimated reliably. Liabilities are recognised at the amount that the charity anticipates it will pay to settle the debt or the amount it has received as advanced payments for the goods or services it must provide. Provisions are measured at the best estimate of the amounts required to settle the obligation.

Trade and other creditors are recognised at the settlement amount after any trade discounts received. Accruals are value based on the estimated amount to be paid.

1.11 Financial instruments

The charity only has financial assets and financial liabilities of a kind that qualify as basic financial instruments. Basic financial instruments are initially recognised at transaction value and subsequently measured at their settlement value.

1.12 Foreign currencies

Monetary assets and liabilities denominated in foreign currencies are translated into sterling at rates of exchange ruling at the balance sheet date.

Transactions in foreign currencies are translated into sterling at the rate ruling on the date of the transaction.

Exchange gains and losses are recognised in the Statement of Financial Activities incorporating Income and Expenditure Account.

1.13 Pensions

The Charity operates a defined contribution pension scheme, and the pension charge represents the amounts payable by the Charity to the fund in respect of the year.

1.14 Fund accounting

General funds are unrestricted funds which are available for use at the discretion of the Trustees in furtherance of the general objectives of the Charity and which have not been designated for other purposes.

Restricted funds are funds which are to be used in accordance with specific restrictions imposed by donors or which have been raised by the Charity for particular purposes. The costs of raising and administering such funds are charged against the specific fund. The aim and use of each restricted fund is set out in the notes to the financial statements.

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

2. Income from donations

	Unrestricted funds 2023	Restricted funds 2023	Total funds 2023
	£	£	£
Donations	-	911	911

	Unrestricted funds 2022	Total funds 2022
	£	£
Donations	3,361	3,361

3. Investment income

	Unrestricted funds 2023	Total funds 2023
	£	£
Investment income	646,024	626,024

	Unrestricted funds 2022	Total funds 2022
	£	£
Investment income	921,274	921,274

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

4. Analysis of expenditure on charitable activities - summary by fund type

	Unrestricted funds 2023	Restricted funds 2023	Total funds 2023
	£	£	£
Charitable activities relating to clinical trials and medical research	4,006,544	911	4,007,455

	Unrestricted funds 2022	Restricted funds 2022	Total funds 2022
	£	£	£
Charitable activities relating to clinical trials and medical research	3,600,515	3,361	3,603,876

5. Analysis of expenditure by activities

	Activities undertaken directly 2023	Support costs 2023	Total funds 2023
	£	£	£
Charitable activities relating to clinical trials and medical research	3,793,649	213,806	4,007,455

	Activities undertaken directly 2022	Support costs 2022	Total funds 2022
	£	£	£
Charitable activities relating to clinical trials and medical research	3,461,644	142,232	3,603,876

These are costs incurred by the Foundation for its charitable purposes and comprise direct costs, which are attributable to a single charitable activity, and support costs, which are not directly attributable to a single charitable activity and are apportioned between charitable activities on a basis consistent with the use of resources.

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

5. Analysis of expenditure by activities (continued)

Analysis of direct costs

	Activities 2023	Total funds 2023
	£	£
Staff Costs	577,683	577,683
Clinical and preclinical research grant and contract costs	3,215,966	3,215,966
	<u>3,793,649</u>	<u>3,793,649</u>

Staff costs comprise wages totalling £496,627 (2022 - £473,469), employers national insurance totalling £56,029 (2022 - £49,614) and pension costs totalling £26,509 (2022 - £47,879).

	Activities 2022	Total funds 2022
	£	£
Staff Costs	572,557	572,557
Research contracts, grants, and other direct costs	2,889,087	2,889,087
	<u>3,461,644</u>	<u>3,461,644</u>

These direct costs are attributable to a single charitable activity.

Analysis of support costs

	Activities 2023	Total funds 2023
	£	£
Staff Costs	126,808	126,808
Depreciation	2,085	2,085
Foreign exchange gain	(6,931)	(6,931)
General costs	44,481	44,481
Legal & professional fees	23,100	23,100
Bank charges	2,530	2,530
Premises costs	-	-
Travel costs	8,533	8,533
Audit fees (governance)	13,200	13,200
Loss on disposal of fixed assets	-	-
	<u>213,806</u>	<u>213,806</u>

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

5. Analysis of expenditure by activities (continued)

Staff costs are made up of wages totalling £108,690 (2022 - £104,283), employers national insurance totalling £12,299 (2022 - £10,891) and pension costs totalling £5,819 (2022 - £10,509).

	Activities 2022	Total funds 2022
	£	£
Staff Costs	125,683	125,683
Depreciation	1,240	1,240
Foreign exchange gain	(160,348)	(160,348)
General costs	106,248	106,248
Legal & professional fees	49,513	49,513
Bank charges	5,571	5,571
Travel costs	2,325	2,325
Audit fees (governance)	12,000	12,000
	<u>142,232</u>	<u>142,232</u>

These support costs are not directly attributable to a single charitable activity and are apportioned between charitable activities on a basis consistent with the use of resources.

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

6. Grants to Institutions

	2023	2022
	£	£
AstraZeneca	56,978	32,705
Biocruces Bizkaia Health Research Institute	1,755	1,798
Boston Children's Hospital	85,618	74,051
Cambridge University	5,557	37,889
Charles River Laboratories International Inc.	773,812	381,890
Children's Hospital of Philadelphia	-	25,712
Developmental Synaptopathies Consortium	47,003	25,309
Evotec International GmbH	1,556,022	1,380,947
Geisel School of Medicine	34,417	-
IDIBELL	-	43,610
Imagen Therapeutics Limited	-	26,234
Institut Josep Carreras	64,776	34,093
John Carroll University	70,886	65,580
Ohio State University	-	15,588
Radboud University Medical Centre	65,704	105,624
Renown Health Foundation	83,246	81,638
The Cleveland Clinic	41,350	74,255
University College London	311,033	365,349
University Hospital Southampton NHS Foundation	8,729	-
University of Melbourne	(21,654)	29,485
	<u>3,185,232</u>	<u>2,801,757</u>

During the year grants were made to institutions in respect of research projects and clinical trials.

These Grants to institutions form part of the Foundation's direct costs, which are costs attributable to a single charitable activity.

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

7. Auditors' remuneration

	2023	2022
	£	£
Fees payable to the Charity's auditor for the audit of the Charity's annual accounts	11,000	10,000
Fees payable to the Charity's auditor in respect of non-audit services	4,289	19,644
	<u> </u>	<u> </u>

Auditor's remuneration forms part of the Foundation's support costs, which are not directly attributable to a single charitable activity and are apportioned between charitable activities on a basis consistent with the use of resources.

8. Staff costs

	2023	2022
	£	£
Wages and salaries	605,643	577,402
Social security costs	68,328	60,505
Other pension costs	32,328	58,388
	<u>706,299</u>	<u>696,295</u>

Staff costs include direct costs, which are attributable to a single charitable activity, and support costs, which are not directly attributable to a single charitable activity and are apportioned between charitable activities on a basis consistent with the use of resources.

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

The average number of persons employed by the Charity during the year was as follows:

	2023	2022
	No.	No.
Research and support staff	7	6

The number of employees whose employee benefits (excluding employer pension costs) exceeded £60,000 was:

	2023	2022
	No.	No.
In the band £60,001 - £70,000	-	1
In the band £70,001 - £80,000	2	-
In the band £80,001 - £90,000	1	-
In the band £110,001 - £120,000	1	2
In the band 160,001 - £170,000	-	1
In the band 170,001 - £180,000	1	-

Transactions with Trustees

During the year, travel expenses of £65 and £27 were reimbursed for Siriana Baldini and Renata Crome, respectively.

Transactions with Key Management Personnel

During the year, the Charity's key management personnel received total remuneration of £528,710 (2022-£568,822). Key management personnel comprised the Chief Executive and Director of Clinical Development, the Director of Translational Medicine, the Director of Research and the Director of Finance and Business Operations.

There were no terminations during the year. (During the previous year ended 31st March 2022, the Charity entered into a settlement agreement, with payments totalling £118,723.)

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

9. Tangible fixed assets

	Computer equipment	Total
Cost or valuation	£	£
At 1 April 2022	8,014	8,014
Additions	1,249	1,249
Disposals	(2,049)	(2,049)
As at 31 March 2023	7,214	7,214
Depreciation		
At 1 April 2022	3,922	3,922
Charge for the year	2,065	2,065
On Disposals	(2,049)	(2,049)
As at 31 March 2022	3,938	3,938
Net book value		
At 31 March 2023	3,276	3,276
At 31 March 2022	4,092	4,092

10. Fixed asset investments

	Listed Investments
Valuation	£
At 1 April 2022	21,817,348
Additions	3,381,205
Disposals	(1,688,575)
Revaluations	(1,182,938)
Transfers between classes	(3,046,785)
Foreign Exchange movement	772,467
At 31 March 2023	20,052,722

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

11. Debtors

Due within one year

	2023	2022
	£	£
Prepayments and accrued income	4,730	4,592
	<u>4,730</u>	<u>4,592</u>

12. Current asset investments

	2023	2022
	£	£
Listed investments	3,745,907	6,223,219
	<u>3,745,907</u>	<u>6,223,219</u>

13. Creditors: Amounts falling due within one year

	2023	2022
	£	£
Trade creditors	12,992	6,478
Other creditors	15,548	2,627
Accruals	753,577	287,005
	<u>782,117</u>	<u>296,110</u>

14. Financial instruments

	2023	2022
	£	£
Financial assets		
Financial assets measured at fair value through income and expenditure	23,798,629	28,040,567
	<u>23,798,629</u>	<u>28,040,567</u>

Financial assets measured at fair value through income and expenditure comprise of fixed and current asset investments.

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

15. Statement of funds

Statement of funds - current year

	Balance at 1 April 2022	Income	Expenditure	Gains/ (Losses)	Balance at 31 March 2023
	£	£	£	£	£
Unrestricted funds					
General Funds	30,150,258	646,024	(4,103,629)	(293,307)	26,399,346
Restricted Funds					
Medical Research	-	911	(911)	-	-
Total	30,150,258	646,935	(4,104,540)	(293,307)	26,399,346

Medical Research - To support medical research taken place into the PTEN gene and finding a potential treatment of PHTS.

Statement of funds – prior year

	Balance at 1 April 2021	Income	Expenditure	Gains/ (Losses)	Balance at 31 March 2022
	£	£	£	£	£
Unrestricted funds					
General Funds	34,212,308	921,274	(3,699,418)	(1,283,906)	30,150,258
Restricted Funds					
Medical Research	-	3,361	(3,361)	-	-
Total	34,212,308	924,635	(3,702,779)	(1,283,906)	30,150,258

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

16. Analysis of net assets between funds

Analysis of net assets between funds - current year

	Unrestricted funds 2023	Total funds 2023
	£	£
Tangible fixed assets	3,276	3,276
Fixed asset investments	20,052,722	20,052,722
Current assets	7,125,465	7,125,465
Creditors due within one year	(782,117)	(782,117)
Total	26,399,346	26,399,346

Analysis of net assets between funds - prior year

	Unrestricted funds 2022	Total funds 2022
	£	£
Tangible fixed assets	4,092	4,092
Fixed asset investments	21,817,348	21,817,348
Current assets	8,624,928	8,624,928
Creditors due within one year	(296,110)	(296,110)
Total	30,150,258	30,150,258

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

17. Reconciliation of net movement in funds to net cash flow from operating activities

	2023	2022
	£	£
Net expenditure for the year (as per Statement of Financial Activities)	(3,750,912)	(4,062,050)
Adjustments for:		
Depreciation charges	2,065	1,240
Loss on disposal	-	1,499
Dividends and interests from investments	(646,024)	(921,274)
(Increase) in debtors	(138)	(147)
Increase/(Decrease) in creditors	486,007	(306,763)
Loss/(gain) on investments	1,217,732	1,905,871
Foreign exchange non-cash movements on investments	(924,425)	(621,965)
Total cash and cash equivalents	(3,615,695)	(4,003,589)

18. Analysis of cash and cash equivalents

	2023	2022
	£	£
Cash at bank	3,374,828	2,397,117
Total cash and cash equivalents	3,374,828	2,397,117

NOTES ON FINANCIAL STATEMENTS
FOR THE YEAR ENDED 31 MARCH 2023

19. Analysis of changes in net debt

	At 1 April 2022	Cash Flows	Other non- cash changes	At 31 March 2023
	£	£	£	£
Cash at bank and in hand	2,397,117	1,141,875	(164,164)	3,374,828
Liquid investments	6,223,219	(2,793,433)	316,121	3,745,907
	8,620,336	(1,651,558)	151,957	7,120,735

20. Pension commitments

The charity operates a defined contribution pension scheme, pension costs for the year were £76,403 (2022 - £58,388). At year end, a balance of £15,546 (2022: £2,627) was due to be paid in respect of pensions.

21. Related party transactions

Apart from the transactions disclosed in note 8, there were no related party transactions in the year.