



## Annual Report 2016

Metrion Biosciences Limited  
Riverside 3, Suite 1  
Granta Park  
Cambridge  
CB21 6AD  
United Kingdom

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## Company Vision

Metribiosciences is a specialist ion channel contract research organisation and drug discovery company. The Company aims to be the leading provider of ion channel assay expertise to the life science industry.

Metribiosciences' corporate goals are:

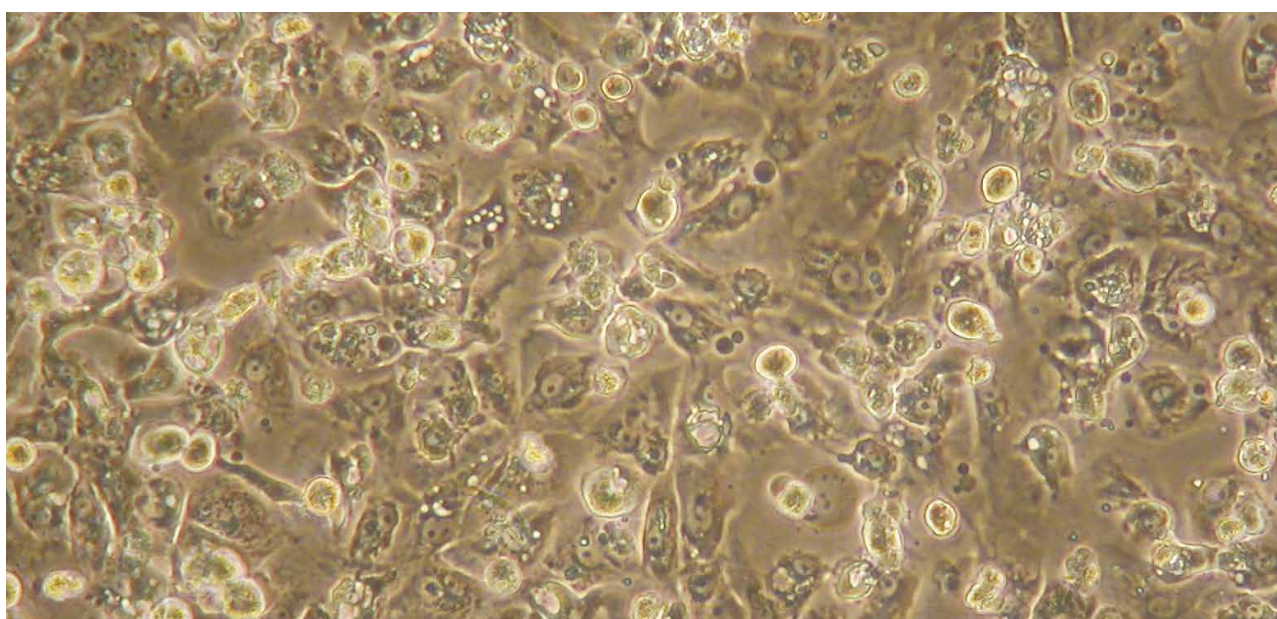
- to enhance pharmaceutical efficacy and safety assessment through the provision of high quality ion channel assays;
- to collaborate with pharmaceutical companies to discover, develop and commercialise novel ion channel medicines; and
- to build a growing and sustainable business for the benefit of shareholders, employees, customers and other stakeholders.

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## Chairman's Statement

Metribiosciences was founded in 2015 as the result of a management buy-out of the research activities and team from Xention Ltd, a venture capital backed ion channel drug discovery company. The Metribiosciences scientific team has more than 100 years of combined expertise in ion channel drug discovery and safety assessment and we are proud to offer some of the highest quality assay services in this field.

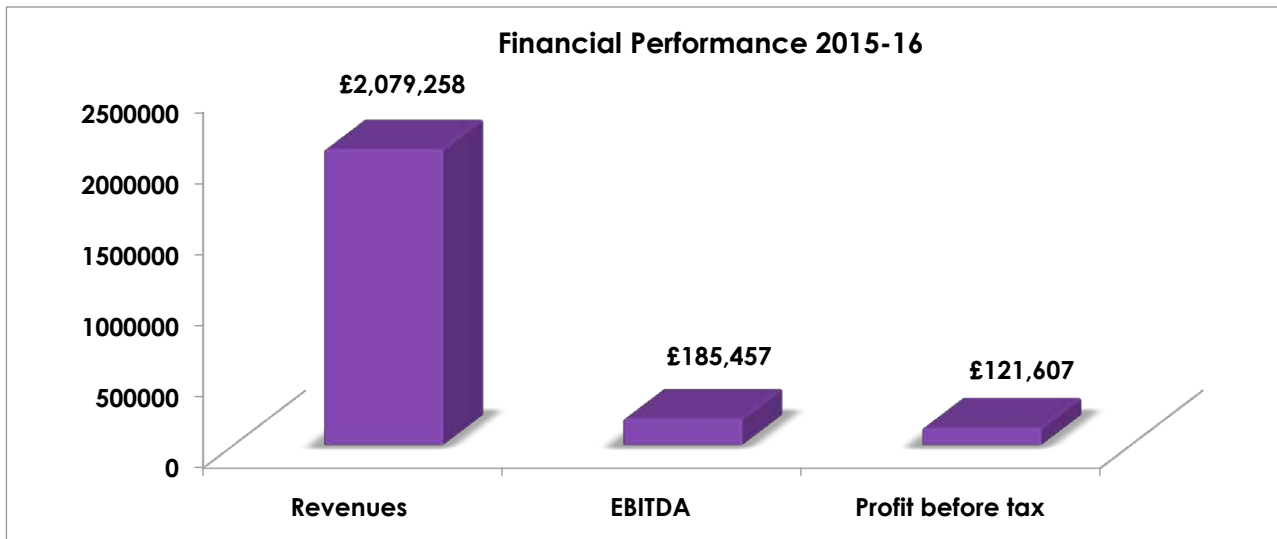
Metribiosciences is committed to assisting pharmaceutical and bio-pharmaceutical companies in harnessing the power of modern ion channel assay technology in the search for and development of new medicines. Whether this be for the purpose of assessing development risks in new compounds or screening compound libraries for selective ion channel modulating compounds, Metribiosciences is well placed to provide detailed and accurate data and advice.



### ***Human induced pluripotent stem cell (iPSC) derived cardiomyocytes in culture.***

Metribiosciences is also working closely with life science companies expert in providing human differentiated cells and tissues from induced pluripotent human stem cells. We are excited by the opportunity to develop and provide our customers with access to stem cell based translational cell and tissue based assays that are expected to be more predictive of the effects of new drug compounds in human clinical studies. The first of these translational assays will be launched by Metribiosciences this year as part of our expanded cardiac safety assessment services.

This Annual Report covers the Company's first financial period from its inception in September 2015 to the end of December 2016. Despite the costs of start-up and moving laboratories in 2016 to the Company's current high quality laboratories at Granta Park, Cambridge, the accounts for the first financial period reflect strong profitable growth.



Total revenues for the period were just over £2 million with EBITDA of £185k (8.9%) and profit before tax of £122k (5.8%). We are pleased with these results but they represent only the first step in building Metrion Biosciences into a world-leading ion channel contract and collaborative research business and high growth company. I look forward to reporting further progress in the coming years.

On behalf of the Company's board of directors, I would like to thank Metrion's employees for their dedication and commitment throughout the year. I would also like to thank our customers, from the UK, Europe and around the world, all of whom we have much enjoyed working with during the year. We look forward to continuing to provide high quality specialist services to the life science marketplace in 2017 and beyond.

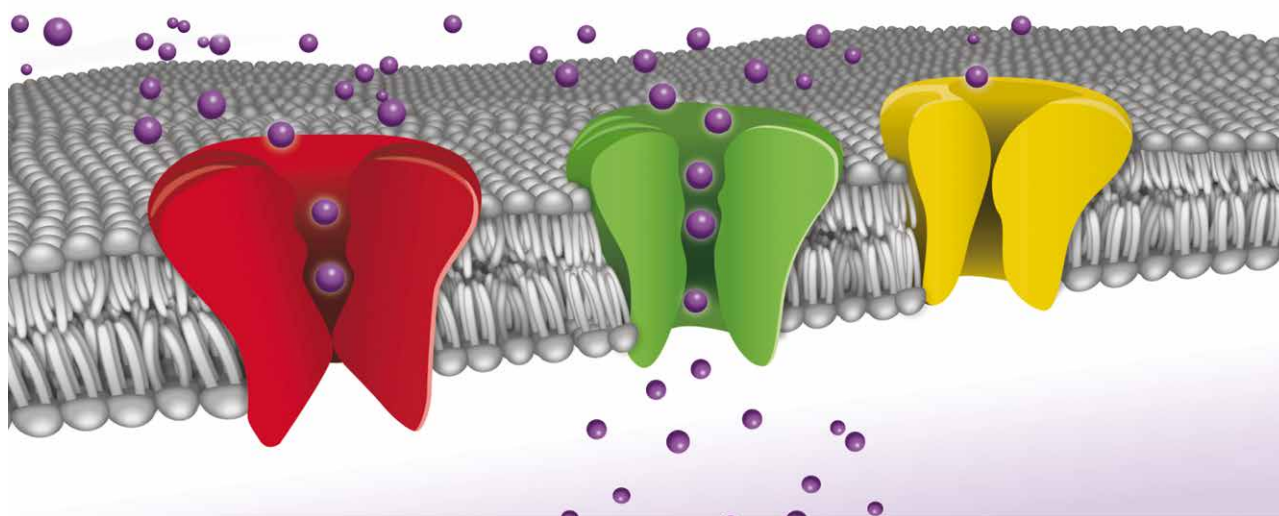
Signature

**Keith McCullagh**  
Chairman, Metrion Biosciences

## Ion Channels in Health and Disease

Ion channels are pore-forming transmembrane proteins that control the flow of ions (electrically charged atoms) across cell membranes. They are involved in multiple cellular functions, including initiation and transmission of nerve signals, enabling muscle contraction and cellular movement, and controlling secretory processes in epithelial and inflammatory cells. Ion channels represent exciting new targets for drug action. The ability to modulate ion channel function selectively has the potential to result in novel treatments for diseases that have so far resisted the reach of new medicines.

However, ion channels are complex proteins with multiple subunits. Their complexity, membrane location and dynamic nature has made understanding their structure and mechanisms of action difficult. Monitoring their function has until recently required labour intensive and challenging manual patch clamp electrophysiological techniques.



**Schematic representation of ions flowing through selected ion channels embedded within a cell membrane (red – closed, green – open, yellow – inactivated).**

Fortunately, the field of ion channel research has advanced rapidly over the last decade, in part due to the highly successful introduction of sophisticated automated assay technologies. In addition, the astonishing growth of genetic information and sequencing techniques has led to a much greater knowledge of ion channel gene families, their protein expression products and characterisation. There are now more than 300 distinct ion channels types identified in human cells and tissues, and genomic data suggests the total number is nearer 500. Many of these specific ion channels have the potential to be selective targets for new drug research programmes.

At the same time, the growth in our understanding of ion channel mechanisms involved in cardiac, neuronal and secretory tissue toxicities now allows more sensitive and predictive safety assessment techniques to be applied to compounds undergoing research and development.

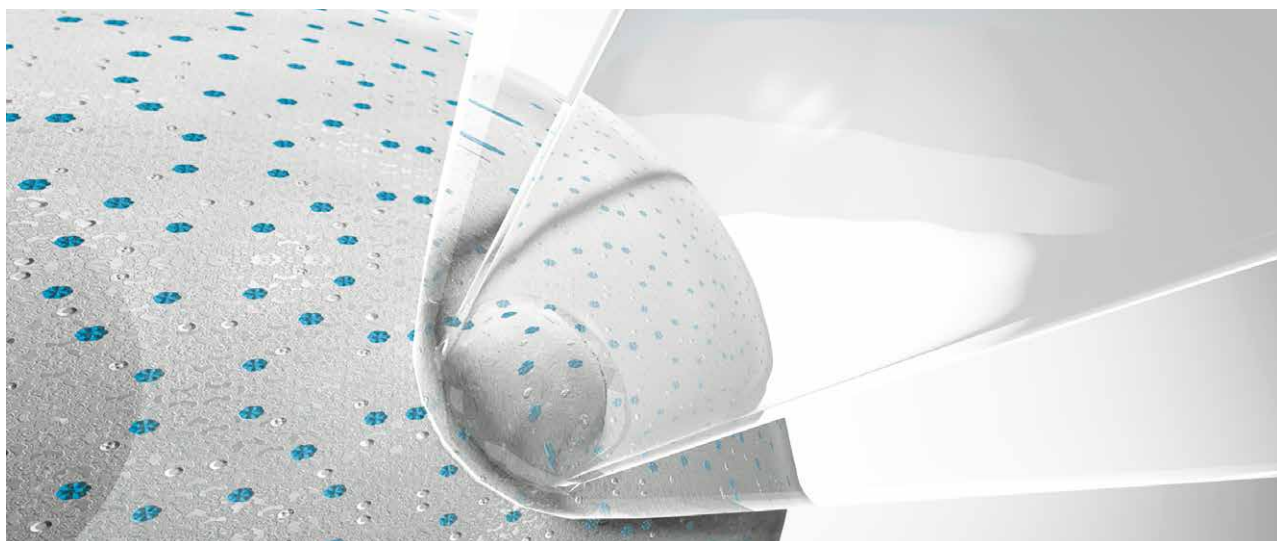


## An Overview of Metrion's Services

The Company's range of services currently encompasses Ion Channel Screening, Cardiac Safety Screening, Neurotoxicology assays, Translational assays and Integrated Drug Discovery, details of which are summarised below.

### (a) Ion Channel Screening

Metrion offers high quality ion channel screening services using a variety of electrophysiology, label free and fluorescence-based platforms. These include conventional manual patch clamp electrophysiology, QPatch and Patchliner automated systems, Axion Maestro and MED 64 microelectrode array technique and FlexStation. Additional capability for fluorescence-based high throughput screening assays, including a 150,000 compound small molecule library, is also available via Metrion's partnership with Assay.Works.



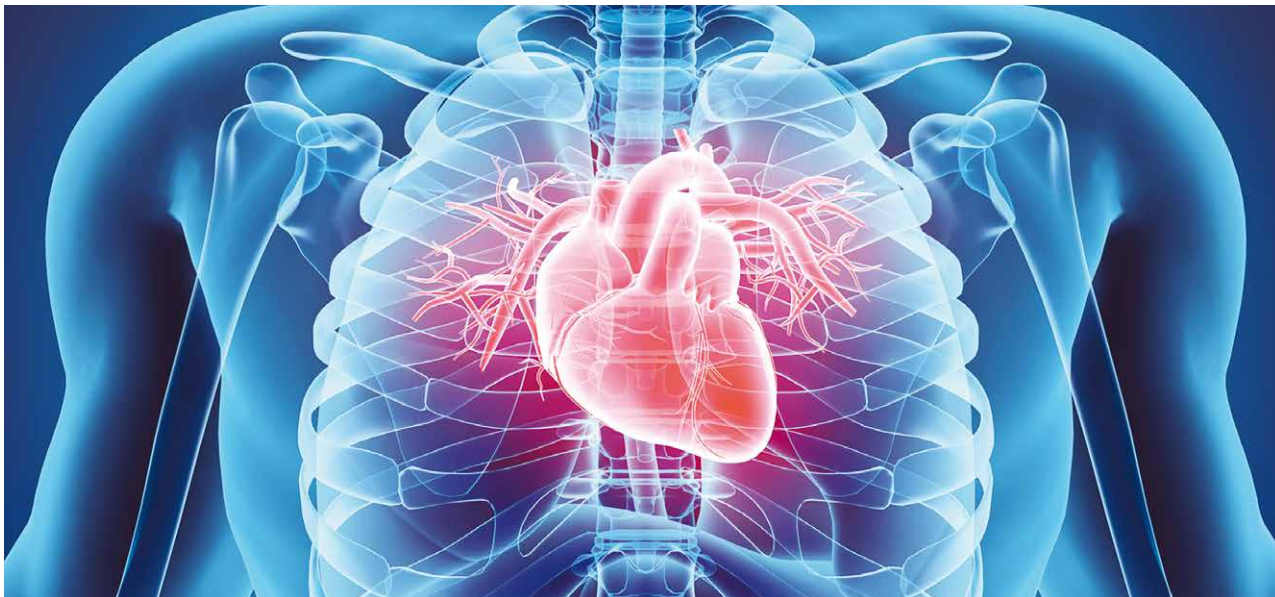
### Schematic representation of a micropipette “clamped” on to an individual cell membrane to measure ion flux.

Ion channel screening services include:

- **Compound screening:** The Company provides compound screening in both single concentration point and concentration-response formats using an in-house library of stable cell lines, client provided cell lines or transiently transfected cells (including baculovirus mediated gene transduction). Detailed biophysical studies, and in-depth interpretation skills, are also available to fingerprint compound mechanism-of-action.
- **Ion Channel Portfolio:** Metrion offers validated ion channel screening services against a wide range of ion channel targets available in-house or from commercial vendors. The Company is continuing to expand its library of ion channel cell lines and is enthusiastic to assist customers with particular ion channels of interest.
- **Cell line optimisation:** Metrion staff have extensive experience of creating, developing, optimising and validating stable cell lines expressing recombinant and endogenous ion channels appropriate for robust ion channel screening assays.
- **Assay development and validation:** Metrion's scientists have many years' experience developing, optimising and validating automated and manual patch clamp assays for ion channel targets. The Company is able to customise ion channel assays at different stages of the screening cascade, from hit finding, through medium throughput structure activity studies, to specialised biophysical and mechanism-of-action studies for hit or lead compounds.

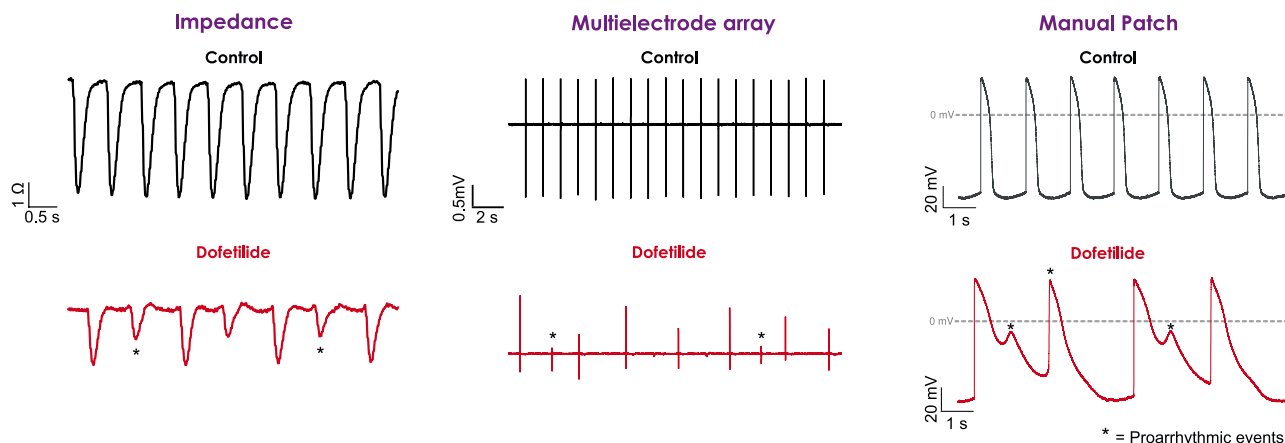
## (b) Cardiac Safety Screening

Metrion provides a suite of cardiac safety screening assays incorporating all three components of the Comprehensive *In vitro* Proarrhythmia Assay (CiPA) initiative. Metrion is a member of the HESI Cardiac Safety committee and a participant in the High Throughput Screening sub-team validating automated screening assays. The company also has access to multiple commercially available iPSC-derived cardiomyocyte cell lines, which have been validated in-house at Metrion.



Metrion's CiPA services include:

- Automated electrophysiology screening against an expanded panel of six cardiac ion channels, including hERG.
- *In silico* modelling using electrophysiology data from the expanded ion channel panel.
- Confirmation of *in silico* predictions using translational assays employing human iPSC-derived cardiomyocytes.



**Metrion has developed a comprehensive panel of iPSC-derived ventricular cardiomyocyte assays.**



### (c) Neuroscience Assays

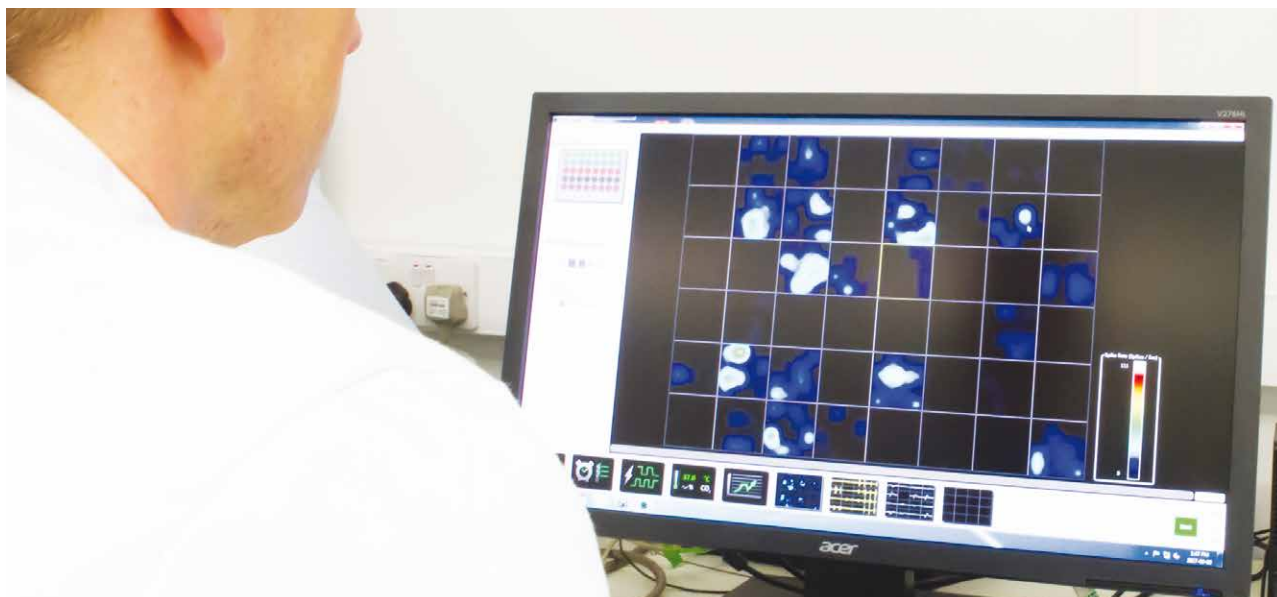


Metrion offers a range of neuroscience-related ion channel screening assays and platforms. Neuronal ion channel screening assays are used to assess the effects of compounds on native ion channel activities, as well as determining central or peripheral neurone firing behaviour. In addition to more general neurotoxicology screening of hits and lead candidates, Metrion has a range of phenotypic assay platforms to enable customers to screen preclinical research compounds for biological responses in cells or tissues, or to provide neurotoxicity safety verification. These bioassays, using technologies, such as manual patch clamp and microelectrode array recordings, can offer a direct read-out of physiological function in native tissue and in rodent or human stem cell-derived neurones (see Translational Assays section below).

### (d) Translational Assays

Metrion phenotypic assays aid the translation of *in vitro* cardiac safety and neuroscience data to more predictive models, enabling the more efficient progression of customer drug discovery programmes. Translational assays often need to be tailored to a client's specific requirements and Metrion's experienced staff are available to discuss and define such requirements. In particular, advice and assays are provided in the following areas:

- **Central Neurone Firing:** Central phenotypic assay platforms at Metrion include manual patch clamp and multi-electrode array (MEA) techniques to establish compound target validation, target engagement and species selectivity. Alternatively, these methods can be used to characterise differentiated cells electrophysiologically.



### **Phenotypic screening using the multi-electrode array (MEA) technique.**

- **Peripheral Neurone Firing:** Metrion utilises peripheral neurone phenotypic assays to enable its customers to assess neuroexcitability or neurosuppression. Physiological activity can be monitored from native tissue such as rodent dorsal root ganglia (DRG) or human DRG.
- **Native Ion Channels:** Metrion is developing screening assays against specific endogenous ion channels expressed within native neurones to provide further compound validation. Determination of the pharmacology and selectivity of compounds in the intact cell milieu can help to bridge the gap between *in vitro* assays and *in vivo* applications. Assays can be designed to explore the mechanism-of-action of compounds, or other specific customer needs.

### **(e) Collaborative Drug Discovery**

Metrion is engaged in a number of current research collaborations with long term customers. In each case, the Company's target knowledge and screening expertise is pivotal in driving the drug discovery programme to a successful outcome. Metrion's experienced project management team ensures that quality and timelines are maintained throughout such client projects, regardless of their size or scope.

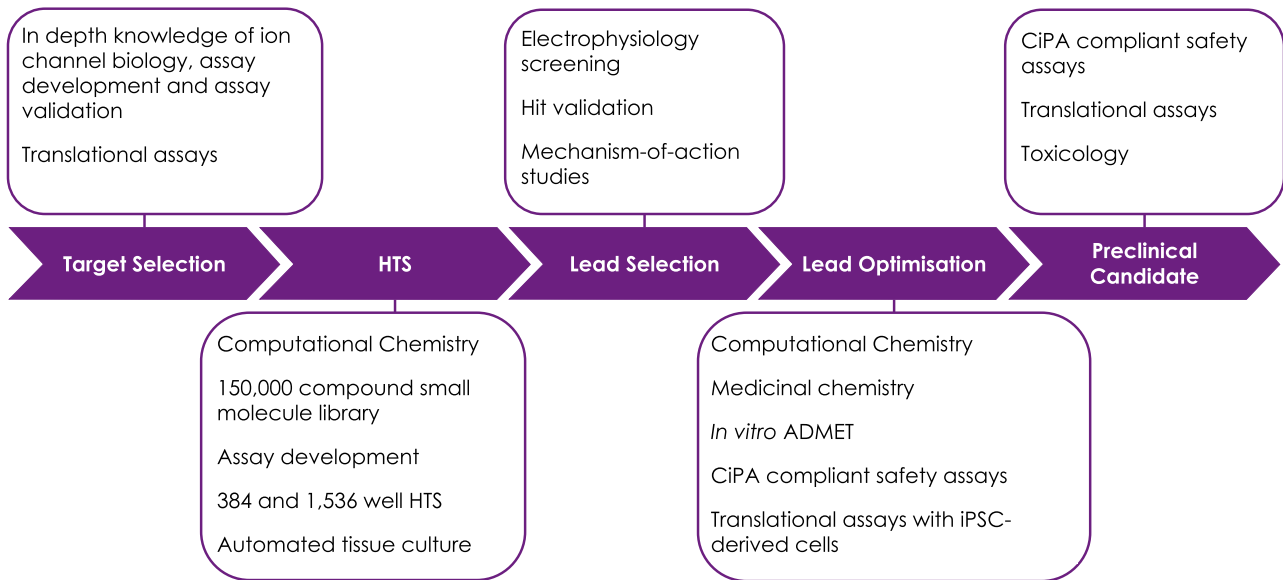
Within the CRO sector, Metrion staff have extensive experience of drug discovery research on behalf of clients based in Europe, USA and Japan, including virtual companies, academic institutions, biotechnology companies and midsize and large pharma businesses. Drug discovery projects managed by Metrion staff have achieved multiple renewals and project milestone payments from clients in each of the geographic regions above. These programmes span a variety of therapeutic areas and have produced development candidates and multiple composition of matter patents.


### (f) Integrated Drug Discovery

By aligning Metrion's expertise with carefully selected partners the Company is also offering an expert fully integrated drug discovery service, including biology, medicinal chemistry and early ADMET. Metrion's integrated research partners are Concept Life Sciences, and Assay Works and together the three companies provide outstanding research experience to steer customer research programmes towards success.

Metrion's chemistry and ADMET partner, Concept Life Sciences, has provided extensive support for Nav1.7 and Nav1.8 programmes over a period of five years, filing 15 patents and publications and a bringing a development candidate to clinical trials.

Metrion has also partnered with Assay.Works, through this partnership we can provide expertise in industry standard plate-based assay development and validation, plus High Throughput Screening (HTS) services of the highest quality for ion channel targets. The Assay.Works team has extensive knowledge of HTS and assay validation technologies, including 384-well format screening and compound handling facilities, a library of 150,000 small molecules and a catalogue of 'assay.ready' cell lines for use in primary screening and selectivity assays.



Integrated drug discovery via Metrion and our partners  

## Internal Research & Development

### (a) Cardiomyocytes

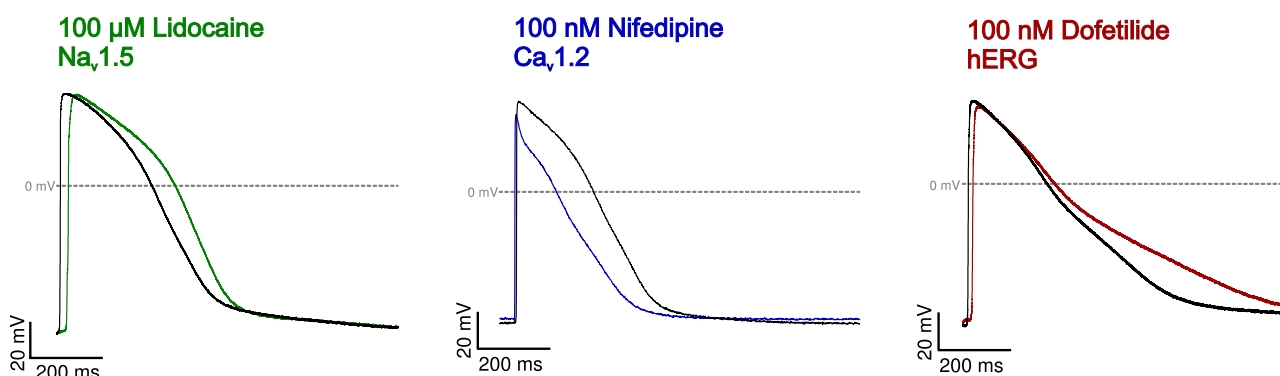
In March 2016, Metrion took up the leadership position in a Eurostars SME consortium to develop stem cell-derived cardiomyocyte reagents, platforms and phenotypic screening assays. With the assistance of Metrion's partners in the consortium, Nanion Technologies (Germany) and Leiden University Medical Center (Netherlands), the Company has developed innovative phenotypic cardiac safety assays, enabling improved evaluation of the proarrhythmic risk of novel therapeutics. The project received funding from the Eurostars-2 joint programme with co-funding from the European Union Horizon 2020 research and innovation programme and Innovate UK, the UK's innovation agency.

The project has used Nanion's CardioExcyte96 platform, which enables simultaneous recording of cardiac cell electrical activity and contractility, to develop Comprehensive *in vitro* Proarrhythmia Assay (CiPA) compliant cardiac safety assays using human iPSC-derived cardiomyocytes developed at Leiden. The resulting proprietary phenotypic assays are expected to be commercialised by Metrion in 2017 and offered to customers, alongside the company's existing CiPA-approved human cardiac ion channel panel and manual patch clamp electrophysiology capabilities.

### (b) iPSC research

In addition to evaluating induced pluripotent stem cell (iPSC)-derived cells from the University of Leiden, Metrion is also working with a number of commercial iPSC-derived cell providers, including Axol Bioscience and Axiogenesis. These alliances are both aimed at improving, and standardising the cell lines available for use in the FDA's CiPA testing initiative.

By combining Metrion's contract research services with human iPSC-derived cells and culture reagents, the Company is also developing other well-validated, stem cell-derived assays and services for use in predictive toxicology and drug discovery screening.



**Pharmacological evaluation of iPSC-derived ventricular cardiomyocytes using the manual patch clamp technique.**



### (c) Human DRG neurones

In August 2016, Metrion entered into a “CrackIT” consortium agreement to evaluate the use of primary human dorsal root ganglion (hDRG) neurones in pain research. As well as Metrion, the consortium partners include the Universities of Glasgow and St Andrews, NHS Greater Glasgow & Clyde, Grünenthal AG and the UK National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), with support and facilitation provided by NHS Blood & Transplant (Scotland). The eventual aim of this project is to enhance research efficiency by putting in place a system whereby high quality and viable human DRG neurones can be supplied to both industrial and academic researchers, thereby partially superseding current methods involving isolated cells or tissues from animals, or *in vivo* animal .



**One of Metrion’s five conventional patch clamp electrophysiology recording systems.**

### (d) Venom peptides

In April 2017, Metrion entered into a research alliance with Venomtech to search for novel venom-derived modulators of therapeutically relevant ion channels. Through this collaboration, Metrion aims to find novel binding sites or new peptides for use in assay validation and eventually innovative drug discovery research. Metrion is seeking partners to further develop this opportunity and welcomes enquiries from interested parties.

Metrion is also conducting other internal research programmes not currently in the public domain, both on its own and in collaboration with undisclosed parties.



## Leadership

### Marc Rogers PhD, Chief Scientific Officer



Marc has extensive experience managing screening projects and outsourcing preclinical drug discovery work, and leads our biology teams for international pharma collaborations and UK and European grant projects. Trained as a physiologist (NZ) and neuroscientist (Australia), Marc undertook an extensive postdoctoral career in the US (Baylor College of Medicine, University of Hawaii, UCSF) training in ion channel biophysics, neurosecretion, and synaptic physiology using a range of patch clamp electrophysiology and fluorescence imaging techniques. He carried out ion channel assay development and automated patch clamp screening at Exelixis in the Bay area before moving to the UK in 2005 to develop ion channel assays on various automated patch clamp platforms (AutoPatch, Patchliner, QPatch) at Xention, specialising in  $\text{Na}_v$ ,  $\text{Ca}_v$  and TRP channels for pain,  $\text{K}_v$  channels in auto-immune disease, and cardiac safety panels.

### Andrew Southan PhD, Chief Operating Officer



Andy has over 25 years' experience in life science research, including 14 years in the CRO sector. In 1991 he received his PhD in Pharmacology from the University of London (UK), investigating the effects of anaesthetics and high pressure on CNS potassium channels. Following a move to industry Andy worked as a brain slice electrophysiologist supporting ion channel-based CNS programmes at Wyeth (UK), before moving to Imperial College London where he published the first patch clamp recordings from cerebellar inhibitory nerve terminals. At CeNeS Pharmaceuticals he performed CRO services (hERG, nAChR) and internal research on HCN and two-pore channels. He subsequently established the electrophysiology laboratory for Ionix Pharmaceuticals, a company focused on identifying novel pain therapeutics, where he worked on  $\text{Na}_v$ ,  $\text{Ca}_v$  and mechanosensitive ion channels. Before joining Metrion, Andy spent 12 years in leadership roles at BioFocus and Charles River managing stand-alone projects, multi-year collaborations and fully integrated drug discovery programmes.

### **Kathy Sutton PhD, Group Leader (Project Manager)**

Kathy has worked in the ion channel field for over 24 years, and has extensive experience in managing and outsourcing ion channel drug discovery projects within both large pharma and the biotech industry. She received her PhD from the University of London (UK) in 1995, characterising voltage gated calcium channels in DRG neurons using the manual patch clamp technique. Kathy continued her interest in Cav channels during postdoctoral research with Terry Snutch at the University of British Columbia (Canada). In 2001, she returned to the UK to work on a number of preclinical pain targets at Parke-Davis (Pfizer) and Merck Sharp and Dohme (Terlings Park). Before joining Metrion, Kathy led internal and external ion channel drug discovery projects at Xention (FLEXStation, FLIPR, Patchliner, QPatch) and was also responsible for managing grant-funded assay development activities (MEA).



### **Robert Kirby PhD, Group Leader (CRO Services)**

Rob is a skilled pharmacologist with over 10 years' experience in ion channel drug discovery. Rob obtained his PhD (Sheffield Hallam, UK) investigating a novel pharmacophore for BK potassium channel openers. At Metrion, Rob leads the team working on a major collaborative drug discovery project with an international pharma company. He also co-ordinates screening activities for CRO work including Metrion's panel of CiPA cardiac assays. Prior to his role at Metrion, Rob spent a year at Drexel University (USA) researching the role of GPCR's in autoimmune disease, after this he was a Principal Scientist at Xention Ltd (UK) where he led screening campaigns on behalf of clients for a variety of ion channel targets (Na<sub>v</sub>1.x, Ca<sub>v</sub>1.x, Ca<sub>v</sub>2.x, K<sub>v</sub>1.x, TRPx, KirX, gIRK, I<sub>Crac</sub>, HCN and hERG) using automated patch clamp electrophysiology (QPatch, PatchLiner) and fluorescence-based screening platforms (FLIPR, FLEXStation).



### **Louise Webdale, Group Leader (Cell Culture Manager)**



Louise has worked in the ion channel field for over 25 years, within both large pharma and biotech industry positions. After obtaining a Biology degree specialising in Mammalian Physiology, she started her career developing diagnostic ELISA kits for the veterinary industry within Cambridge Life Sciences. Following this, she joined the Assay Development group at Parke-Davis Neuroscience Research Centre (Pfizer), Cambridge, where she was a founding member of the Cell Culture Department and over a period of 11 years supplied reagents to support projects within the Cambridge and Sandwich sites. She then moved to Cytomyx (Millipore) to create the Cell Culture Department and was fundamental in the developing of over 120 ion channel and GPCR cell lines, sold worldwide under the PrecisION™ trademark. Since 2009, Louise has continued her interest in ion channel biology, initially at Xention Discovery and more recently at Metrion where she is Cell Culture Manager. Current responsibilities include supplying cell reagents to support all internal and CRO based projects using recombinant expression systems, primary cell lines and Induced Pluripotent Stem cells (iPSCs).

### **Tony Rush PhD, Senior Scientist II (Neuroscience and Translational Assays)**



Tony has been an ion channel researcher for over 20 years across academia and industry and is widely published in the area. He received his PhD from the University of Dundee (UK) characterising sodium channels of DRG neurones using the patch clamp technique. He then studied hippocampal synaptic plasticity at Trinity College Dublin (Ireland), before continuing sodium channel research with Stephen Waxman at Yale University (USA). Subsequently, Tony co-ordinated ion channel contracts at NeuroSolutions Ltd (UK), taking projects on multiple targets from initial discussions through to completion for a wide variety of clients in the biotechnology and pharmaceutical industries. He moved to AstraZeneca (Sweden) to work on preclinical pain targets where he was lead biologist for a number of ion channel programmes and large scale screens (IonWorks, QPatch, manual patch). Tony returned to the UK where he worked on ion channel screening projects (Patchliner) and translational neuroscience assays (MEA, manual patch) for external partners and grant-based projects firstly at Xention, and now at Metrion.

## **John Ridley PhD, Business Manager**

John has a dual role at Metrion that involves supporting our business development activities and performing electrophysiology studies in the lab. John holds a PhD in cardiac electrophysiology from the University of Bristol and an MPhil in Bioscience Enterprise from the University of Cambridge. He has 10 years' experience working in ion channel drug discovery. This experience was obtained firstly as a Senior Scientist at Xention, where he was involved in the discovery of ion channel blockers for atrial fibrillation, neuropathic pain and autoimmune diseases, and then as the Business Development Manager at Xention. John is also the Business Development Director for Cambridge Animal Health, which is a company that is dedicated to developing a non-surgical technology to neuter cats and dogs of both sexes.





## Board of Directors

### Keith McCullagh PhD, Non-executive Chairman



Keith McCullagh is an experienced bioscience entrepreneur and is also chairman of Xention, Ario Pharma and Torpedo Factory Group. He was previously chairman of Affitech, Pharmacy 2U and Clavis Pharma and from 2004 to 2008 was Chief Executive of Santaris Pharma, an RNA medicines company sold to Roche in 2014. From 1986 to 1998, Keith was Chief Executive of British Biotech, now Vernalis, a company he founded and built into one of Europe's first public biopharmaceutical businesses. Prior to British Biotech, he was UK Research Director for GD Searle & Co, Inc., now part of Pfizer.

### Marc Rogers PhD, Founding Director and Chief Scientific Officer



Marc has 25 years' experience in the patch clamp technique and 12 years of drug discovery on both sides of the Atlantic. He was an early adopter of automated patch clamp platforms for ion channel screening and has an excellent knowledge of this market and connections with many of the commercial vendors. Marc has developed an extensive network of contacts in Europe and the US through his outsourcing activities and presentations at international ion channel drug discovery conferences. He is an experienced project manager and team leader through his work on international pharma and grant-funded collaborations, as well as a successful grant writer in the UK, Europe and the US. Before becoming the founding director of Metrion he co-founded the virtual biotech Inovion Pharma to focus on finding therapies for rare disease channelopathies.



### John Ford PhD, Investor Director

John obtained his PhD at the University of Leeds and has almost 20 years of fundraising, ion channel, drug discovery and drug development experience. John is also CEO of Ario Pharma where he leads programs designed to develop TRP channel drugs for pain and CEO of Enterprise Therapeutics, a company evaluating novel therapies for respiratory disease. He was a co-founder of Xention Discovery Ltd. and responsible for the Kv1.5 ion channel atrial fibrillation project subsequently partnered to Servier (up to 120M EUR). Recently, John was a member of the Executive Team at Dezima that developed TA-8995 for dyslipidaemia (The Lancet) and sold the company to Amgen (\$300M upfront, potential deal size of US\$1.55bn + royalties).



### Nick Tait, Finance Director and Company Secretary

Nick graduated from the University of Warwick with a degree in Economics in 1993, he then trained with Ernst & Young (EY) in London, becoming a Chartered Accountant in 1998. Clients at EY included Polygram, Warner Music, Legoland Windsor, BP and Whitbread. He joined Whitbread in 1998, working in the Corporate, Pubs and Bars (where he was a key part of the disposal work to Laurel Pub Company in 2001), and David Lloyd Leisure divisions. In 2002, he co-founded and was Finance Director of The Great Little Pub Company, and during his time there also undertook project assignments at Aviva, Acambis, and SIG Group. He was Head of Finance at Black Trace Group from 2006 to 2012, being instrumental in its expansion overseas to the US, Japan, India and Brazil. He was part of the team that sold Qype to Yelp in 2013, and was CFO of Ranier Technology in Cambridge until 2015, where he oversaw 2 funding rounds and also helped gain Venture Debt funding for the business. He is currently Associate Director of Denovo Partners Ltd., helping Technology and Life Science SMEs set-up, grow and manage their finance, HR and administrative burdens.



Registered number: 09669815

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**METRION BIOSCIENCES LIMITED**

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**DIRECTORS' REPORT AND FINANCIAL STATEMENTS**

**FOR THE PERIOD ENDED 31 DECEMBER 2016**

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**METRION BIOSCIENCES LIMITED**

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**COMPANY INFORMATION**

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<b>DIRECTORS</b>	J W Ford K G McCullagh M Rogers N A J Tait
<b>COMPANY SECRETARY</b>	N A J Tait
<b>REGISTERED NUMBER</b>	09669815
<b>REGISTERED OFFICE</b>	Suite 1 3 Riverside Granta Park Abington Cambridge CB21 6AD
<b>INDEPENDENT AUDITORS</b>	Peters Elworthy & Moore Chartered Accountants & Statutory Auditors Salisbury House Station Road Cambridge CB1 2LA

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**METRION BIOSCIENCES LIMITED**

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**METRION BIOSCIENCES LIMITED**

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**DIRECTORS' REPORT  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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The directors present their report and the financial statements for the period ended 31 December 2016.

**PRINCIPAL ACTIVITY**

The company was incorporated on 3 July 2015. During the period, the company's principal activity was ion channel contract research and collaborative drug discovery services for the pharmaceutical and life sciences industry.

**DIRECTORS**

The directors who served during the period were:

J W Ford (appointed 1 December 2015)  
K G McCullagh (appointed 1 December 2015)  
M Rogers (appointed 3 July 2015)  
N A J Tait (appointed 1 December 2015)

**DIRECTORS' RESPONSIBILITIES STATEMENT**

The directors are responsible for preparing the Directors' report and the financial statements in accordance with applicable law and regulations.

Company law requires the directors to prepare financial statements for each financial year. Under that law the directors have elected to prepare the financial statements in accordance with applicable law and United Kingdom Accounting Standards (United Kingdom Generally Accepted Accounting Practice), including Financial Reporting Standard 102 'The Financial Reporting Standard applicable in the UK and Republic of Ireland'. Under company law the directors 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 company and of the profit or loss of the company for that period. In preparing these financial statements, the directors are required to:

- select suitable accounting policies for the company's financial statements and then apply them consistently;
- 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 company will continue in business.

The directors are responsible for keeping adequate accounting records that are sufficient to show and explain the company's transactions and disclose with reasonable accuracy at any time the financial position of the 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 company and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.



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**METRION BIOSCIENCES LIMITED**

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**DIRECTORS' REPORT (CONTINUED)  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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**DISCLOSURE OF INFORMATION TO AUDITORS**

Each of the persons who are directors at the time when this Directors' report is approved has confirmed that:

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

**AUDITORS**

The auditors, Peters Elworthy & Moore, will be proposed for reappointment in accordance with section 485 of the Companies Act 2006.

**SMALL COMPANIES NOTE**

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

This report was approved by the board and signed on its behalf.



**K G McCullagh**  
Director

Date: 6 March 2017

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**METRION BIOSCIENCES LIMITED**

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**INDEPENDENT AUDITORS' REPORT TO THE SHAREHOLDERS OF METRION BIOSCIENCES LIMITED**

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We have audited the financial statements of Metrion Biosciences Limited for the period ended 31 December 2016, set out on pages 5 to 14. The relevant financial reporting framework that has been applied in their preparation is the Companies Act 2006 and the United Kingdom Accounting Standards (United Kingdom Generally Accepted Accounting Practice), including Financial Reporting Standard 102 'The Financial Reporting Standard applicable in the UK and Republic of Ireland'.

This report is made solely to the 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 company's members those matters we are required to state to them in an Auditors' 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 company and the company's members as a body, for our audit work, for this report, or for the opinions we have formed.

**RESPECTIVE RESPONSIBILITIES OF DIRECTORS AND AUDITORS**

As explained more fully in the Directors' responsibilities statement on page 1, the directors are responsible for the preparation of the financial statements and for being satisfied that they give a true and fair view. Our responsibility is to audit and express an opinion on the financial statements in accordance with applicable law and International Standards on Auditing (UK and Ireland). Those standards require us to comply with the Financial Reporting Council's Ethical Standards for Auditors.

**SCOPE OF THE AUDIT OF THE FINANCIAL STATEMENTS**

An audit involves obtaining evidence about the amounts and disclosures in the financial statements sufficient to give reasonable assurance that the financial statements are free from material misstatement, whether caused by fraud or error. This includes an assessment of whether the accounting policies are appropriate to the company's circumstances and have been consistently applied and adequately disclosed; the reasonableness of significant accounting estimates made by the directors; and the overall presentation of the financial statements. In addition, we read all the financial and non-financial information in the Directors' report to identify material inconsistencies with the audited financial statements and to identify any information that is apparently materially incorrect based on, or materially inconsistent with, the knowledge acquired by us in the course of performing the audit. If we become aware of any apparent material misstatements or inconsistencies we consider the implications for our report.

**OPINION ON FINANCIAL STATEMENTS**

In our opinion the financial statements:

- give a true and fair view of the state of the company's affairs as at 31 December 2016 and of its profit or loss for the period 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.

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**METRION BIOSCIENCES LIMITED**

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**INDEPENDENT AUDITORS' REPORT TO THE SHAREHOLDERS OF METRION BIOSCIENCES LIMITED  
(CONTINUED)**

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**OPINION ON OTHER MATTER PRESCRIBED BY THE COMPANIES ACT 2006**

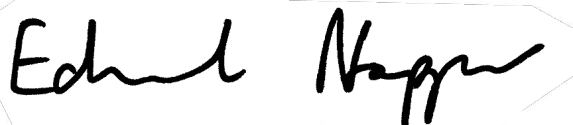
In our opinion, based on the work undertaken in the course of the audit, the information given in the Directors' report for the financial period for which the financial statements are prepared is consistent with those financial statements and this report has been prepared in accordance with applicable legal requirements.

In the light of our knowledge and understanding of the company and its environment obtained in the course of the audit, we have not identified material misstatements in the Directors' report.

**MATTERS ON WHICH WE ARE REQUIRED TO REPORT BY EXCEPTION**

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

- adequate accounting records have not been kept, or returns adequate for our audit have not been received from branches not visited by us; or
- the financial statements are not in agreement with the accounting records and returns; or
- certain disclosures of directors' remuneration specified by law are not made; or
- we have not received all the information and explanations we require for our audit; or
- the directors were not entitled to take advantage of the small companies' exemption from the requirement to prepare a Strategic report or in preparing the Directors' report.



Edward Napper (Senior statutory auditor)

for and on behalf of  
**Peters Elworthy & Moore**

Chartered Accountants  
Statutory Auditors

Salisbury House  
Station Road  
Cambridge  
CB1 2LA

9 March 2017

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**METRION BIOSCIENCES LIMITED**

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**PROFIT AND LOSS ACCOUNT  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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	Note	2016 £
Turnover	3	2,079,258
Cost of sales		(298,503)
<b>GROSS PROFIT</b>		<u>1,780,755</u>
Administrative expenses		(1,658,152)
<b>OPERATING PROFIT</b>		<u>122,603</u>
Interest receivable and similar income		214
Interest payable and similar expenses		(1,210)
<b>PROFIT BEFORE TAX</b>		<u>121,607</u>
Tax on profit		-
<b>PROFIT FOR THE PERIOD</b>		<u><u>121,607</u></u>

The notes on pages 7 to 14 form part of these financial statements.

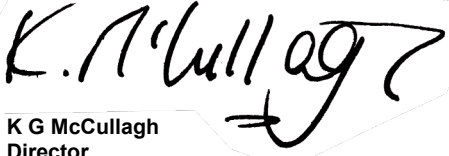
**METRION BIOSCIENCES LIMITED**  
**REGISTERED NUMBER: 09669815**

**BALANCE SHEET**  
**AS AT 31 DECEMBER 2016**

	Note		2016 £
<b>FIXED ASSETS</b>			
Intangible assets	7		29,000
Tangible assets	8		261,764
			290,764
<b>CURRENT ASSETS</b>			
Stocks	9	33,836	
Debtors: amounts falling due within one year	10	365,504	
Cash at bank and in hand		269,591	
		668,931	
Creditors: amounts falling due within one year	11	(258,060)	
			410,871
<b>NET CURRENT ASSETS</b>			
			701,635
<b>TOTAL ASSETS LESS CURRENT LIABILITIES</b>			
Creditors: amounts falling due after more than one year	12		(335,658)
			365,977
<b>NET ASSETS</b>			
			365,977
<b>CAPITAL AND RESERVES</b>			
Called up share capital	13		2,612
Share premium account			241,758
Profit and loss account			121,607
			365,977

The financial statements have been prepared in accordance with the provisions applicable to companies subject to the small companies' regime and in accordance with the provisions of FRS 102 Section 1A - small entities.

The financial statements were approved and authorised for issue by the board and were signed on its behalf by:

  
**K G McCullagh**  
 Director

Date: 6 March 2017

The notes on pages 7 to 14 form part of these financial statements.



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**METRION BIOSCIENCES LIMITED**

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**NOTES TO THE FINANCIAL STATEMENTS  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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**1. GENERAL INFORMATION**

The company is limited by shares and incorporated in England. The address of the registered office is given on the Company Information page of these financial statements.

**2. ACCOUNTING POLICIES****2.1 BASIS OF PREPARATION OF FINANCIAL STATEMENTS**

The financial statements have been prepared under the historical cost convention unless otherwise specified within these accounting policies and in accordance with Section 1A of Financial Reporting Standard 102, the Financial Reporting Standard applicable in the UK and the Republic of Ireland and the Companies Act 2006.

The following principal accounting policies have been applied:

**2.2 TURNOVER**

Turnover comprises revenue recognised by the company in respect of contract research services supplied during the period and grant income, exclusive of Value Added Tax.

Grants of revenue nature are recognised in the Profit and loss account in the same period as the related expenditure.

**2.3 INTANGIBLE ASSETS**

Intangible assets are initially recognised at cost. After recognition, under the cost model, intangible assets are measured at cost less any accumulated amortisation and any accumulated impairment losses.

All intangible assets are considered to have a finite useful life. If a reliable estimate of the useful life cannot be made, the useful life shall not exceed ten years.

**2.4 TANGIBLE FIXED ASSETS**

Tangible fixed assets under the cost model are stated at historical cost less accumulated depreciation and any accumulated impairment losses. Historical cost includes expenditure that is directly attributable to bringing the asset to the location and condition necessary for it to be capable of operating in the manner intended by management.

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**METRION BIOSCIENCES LIMITED**

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**NOTES TO THE FINANCIAL STATEMENTS  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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**2. ACCOUNTING POLICIES (CONTINUED)****2.4 TANGIBLE FIXED ASSETS (CONTINUED)**

Depreciation is charged so as to allocate the cost of assets less their residual value over their estimated useful lives, using the straight line method.

The estimated useful lives range as follows:

Short-term leasehold property	- Over the period of the lease
Plant and machinery	- 33% straight line
Office equipment	- 33% straight line
Computer equipment	- 33% straight line

The assets' residual values, useful lives and depreciation methods are reviewed, and adjusted prospectively if appropriate, or if there is an indication of a significant change since the last reporting date.

Gains and losses on disposals are determined by comparing the proceeds with the carrying amount and are recognised in the Profit and loss account.

**2.5 STOCKS**

Stocks are stated at the lower of cost and net realisable value.

**2.6 DEBTORS**

Short term debtors are measured at transaction price, less any impairment. Loans receivable are measured initially at fair value, net of transaction costs, and are measured subsequently at amortised cost using the effective interest method, less any impairment.

**2.7 CASH AND CASH EQUIVALENTS**

Cash is represented by cash in hand and deposits with financial institutions repayable without penalty on notice of not more than 24 hours. Cash equivalents are highly liquid investments that mature in no more than three months from the date of acquisition and that are readily convertible to known amounts of cash with insignificant risk of change in value.

**2.8 CREDITORS**

Short term creditors are measured at the transaction price. Other financial liabilities, including bank loans, are measured initially at fair value, net of transaction costs, and are measured subsequently at amortised cost using the effective interest method.

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**METRION BIOSCIENCES LIMITED**

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**NOTES TO THE FINANCIAL STATEMENTS  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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**2. ACCOUNTING POLICIES (CONTINUED)****2.9 FOREIGN CURRENCY TRANSLATION****Functional and presentation currency**

The company's functional and presentational currency is GBP.

**Transactions and balances**

Foreign currency transactions are translated into the functional currency using the spot exchange rates at the dates of the transactions.

At each period end foreign currency monetary items are translated using the closing rate. Non-monetary items measured at historical cost are translated using the exchange rate at the date of the transaction and non-monetary items measured at fair value are measured using the exchange rate when fair value was determined.

Foreign exchange gains and losses resulting from the settlement of transactions and from the translation at period-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognised in the Profit and loss account except when deferred in other comprehensive income as qualifying cash flow hedges.

Foreign exchange gains and losses that relate to borrowings and cash and cash equivalents are presented in the Profit and loss account within 'finance income or costs'. All other foreign exchange gains and losses are presented in the Profit and loss account within 'other operating income'.

**2.10 OPERATING LEASES**

Rentals paid under operating leases are charged to the Profit and loss account on a straight line basis over the lease term.

Benefits received and receivable as an incentive to sign an operating lease are recognised on a straight line basis over the lease term, unless another systematic basis is representative of the time pattern of the lessee's benefit from the use of the leased asset.

**2.11 PENSIONS****DEFINED CONTRIBUTION PENSION PLAN**

The company operates a defined contribution plan for its employees. A defined contribution plan is a pension plan under which the company pays fixed contributions into a separate entity. Once the contributions have been paid the company has no further payment obligations.

The contributions are recognised as an expense in the Profit and loss account when they fall due. Amounts not paid are shown in accruals as a liability in the Balance sheet. The assets of the plan are held separately from the company in independently administered funds.

**2.12 INTEREST INCOME**

Interest income is recognised in the Profit and loss account using the effective interest method.

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**METRION BIOSCIENCES LIMITED**

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**NOTES TO THE FINANCIAL STATEMENTS  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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**2. ACCOUNTING POLICIES (CONTINUED)**

**2.13 BORROWING COSTS**

All borrowing costs are recognised in the Profit and loss account in the period in which they are incurred.

**2.14 TAXATION**

Tax is recognised in the Profit and loss account, except that a charge attributable to an item of income and expense recognised as other comprehensive income or to an item recognised directly in equity is also recognised in other comprehensive income or directly in equity respectively.

The current income tax charge is calculated on the basis of tax rates and laws that have been enacted or substantively enacted by the balance sheet date in the countries where the company operates and generates income.

**2.15 RESEARCH AND DEVELOPMENT**

Research and development expenditure is recognised in the Profit and loss account in the period in which they are incurred.

**3. TURNOVER**

An analysis of turnover by class of business is as follows:

	<b>2016</b>
	<b>£</b>
Contract research services	<b>1,888,126</b>
Grant income	<b>191,132</b>
	<b><u>2,079,258</u></b>

**4. AUDITORS' REMUNERATION**

	<b>2016</b>
	<b>£</b>
Fees payable to the company's auditor for the audit of the company's annual financial statements	<b>4,000</b>
	<b><u>4,000</u></b>

**5. EMPLOYEES**

The average monthly number of employees, including directors, during the period was 12.

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**METRION BIOSCIENCES LIMITED**

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**NOTES TO THE FINANCIAL STATEMENTS  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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**6. TAXATION**

No taxation arises as a result of the taxable loss for the period.

**7. INTANGIBLE ASSETS**

	Cell lines £
<b>COST</b>	
Additions	30,000
At 31 December 2016	<u>30,000</u>
<b>AMORTISATION</b>	
Charge for the year	1,000
At 31 December 2016	<u>1,000</u>
<b>NET BOOK VALUE</b>	
At 31 December 2016	<u><u>29,000</u></u>

**8. TANGIBLE FIXED ASSETS**

	Short-term leasehold property £	Plant and machinery £	Office equipment £	Computer equipment £	Total £
<b>COST OR VALUATION</b>					
Additions	97,004	222,167	2,861	1,582	323,614
At 31 December 2016	<u>97,004</u>	<u>222,167</u>	<u>2,861</u>	<u>1,582</u>	<u>323,614</u>
<b>DEPRECIATION</b>					
Charge for the period on owned assets	5,105	55,894	711	140	61,850
At 31 December 2016	<u>5,105</u>	<u>55,894</u>	<u>711</u>	<u>140</u>	<u>61,850</u>
<b>NET BOOK VALUE</b>					
At 31 December 2016	<u><u>91,899</u></u>	<u><u>166,273</u></u>	<u><u>2,150</u></u>	<u><u>1,442</u></u>	<u><u>261,764</u></u>



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**METRION BIOSCIENCES LIMITED**


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**NOTES TO THE FINANCIAL STATEMENTS  
FOR THE PERIOD ENDED 31 DECEMBER 2016**


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**8. TANGIBLE FIXED ASSETS (CONTINUED)**

The net book value of land and buildings may be further analysed as follows:

	2016 £
Short leasehold	91,899
	<u>91,899</u>

**9. STOCKS**

	2016 £
Consumables	33,836
	<u>33,836</u>

**10. DEBTORS**

	2016 £
Trade debtors	195,013
Other debtors	32,210
Prepayments and accrued income	138,281
	<u>365,504</u>

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**METRION BIOSCIENCES LIMITED**

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**NOTES TO THE FINANCIAL STATEMENTS  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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**11. CREDITORS: AMOUNTS FALLING DUE WITHIN ONE YEAR**

	2016 £
Bank loans	32,238
Trade creditors	147,530
Other taxation and social security	18,169
Other creditors	11,802
Accruals and deferred income	48,321
	258,060

Bank loans are transacted on a repayment basis, bear interest at 2.95% over Bank of England base rate and are secured by a first legal charge over the company's assets.

**12. CREDITORS: AMOUNTS FALLING DUE AFTER MORE THAN ONE YEAR**

	2016 £
Bank loans	57,258
Other loans	278,400
	335,658

**Secured loans**

Bank loans are transacted on a repayment basis, bear interest at 2.95% over Bank of England base rate and are secured by a first legal charge over the company's assets.

Other loans are transacted on a interest only basis, bear interest at 2.95% over Bank of England base rate and are secured by a charge over the company's assets.

**13. SHARE CAPITAL**

	2016 £
<b>SHARES CLASSIFIED AS EQUITY</b>	
<b>ALLOTTED, CALLED UP AND FULLY PAID</b>	
261,200 Ordinary shares shares of £0.01 each	2,612

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**METRION BIOSCIENCES LIMITED**

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**NOTES TO THE FINANCIAL STATEMENTS  
FOR THE PERIOD ENDED 31 DECEMBER 2016**

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**13. SHARE CAPITAL (CONTINUED)**

On incorporation the company issued 1 ordinary share with a nominal value of £0.01 at par.

On 30 September 2015 the company issued 16,999 ordinary shares with a nominal value of £0.01 at par.

On 2 December 2015 the company issued 244,200 ordinary shares with a nominal value of £0.01 for consideration of £244,200.

**14. PENSION COMMITMENTS**

The company operates a defined contributions pension scheme. The assets of the scheme are held separately from those of the company in an independently administered fund. The pension cost charge represents contributions payable by the company to the fund and amounted to £101,338. At the balance sheet date, unpaid contributions of £7,952 were due to the fund, which are included within other creditors.

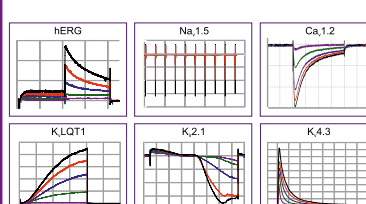
**15. COMMITMENTS UNDER OPERATING LEASES**

At 31 December 2016 the company had future minimum lease payments under non-cancellable operating leases as follows:

	<b>2016 £</b>
Less than 1 year	<b>128,509</b>
1 - 5 years	<b>460,490</b>
	<hr/> <b>588,999</b> <hr/>



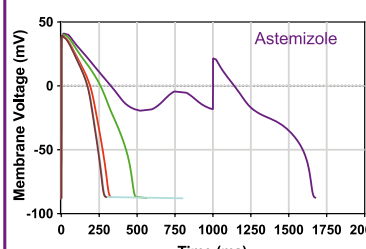
### Human Cardiac Channels



Panel of validated Comprehensive *In Vitro* Proarrhythmia (CiPA) compliant assays.

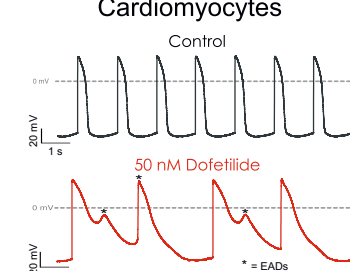
Gigaseal quality automated patch clamp platforms, including QPatch 48 and Patchliner.

### *In Silico* Modelling



Patch clamp data enables accurate *in silico* modelling of the effects of compounds on human ventricular action potentials.

### Human iPSC-derived Cardiomyocytes



Electrophysiology assays using human iPSC-derived cardiomyocytes can confirm *in silico* modelling findings.

Predict Proarrhythmia with Metrion's Complete **CiPA** Toolkit

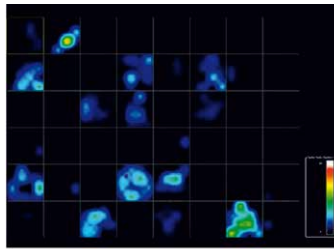
info@metrionbiosciences.com

Tel: +44 (0) 1223 919 100

www.metrionbiosciences.com/  
services/cardiac-safety-screening/



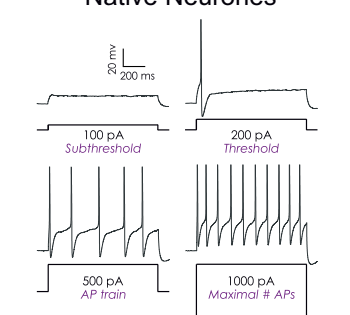
### Multi-electrode array (MEA)



MEA enables fingerprinting of neuronal firing in native and iPSC-derived cells over days or even months.

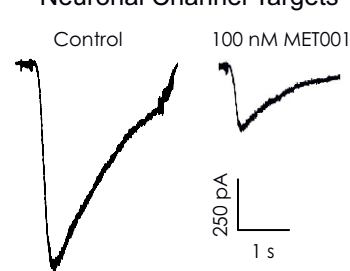
Non-invasive monitoring of neuronal activity to verify compound action or assess toxicity effects.

### Native Neurons



Use of current clamp to evaluate passive membrane properties and firing behaviour in individual neurones.

### Neuronal Channel Targets



Endogenous ion channel assays using native cells to provide further compound validation.

Custom assay formats available to explore compound mechanism-of-action.

Ask About Our Range of Translational Assays and Platforms

info@metrionbiosciences.com

Tel: +44 (0) 1223 919 100

www.metrionbiosciences.com/  
services/translational-neuroscience/



# The Ion Channel Specialists Ion Channel Screening



### Compound Screening

QPatch and Patchliner automated electrophysiology  
Conventional electrophysiology, impedance, microelectrode array and fluorescence assays  
Routine profiling, biophysical analysis

### Cell Line Optimisation

Vendor Na<sub>v</sub>1.8 cell line      Metribiosciences optimised cells 'Condition D'

Metribiosciences' optimised conditions reliably improve recording success rate

Condition	% Success Rate
Original	~40%
A	~50%
B	~60%
C	~65%
D	~85%

Optimisation of functional expression level and homogeneity in challenging cell lines

### Custom Assay Development and Validation

Voltage-gated ion channel assays

Ligand-gated ion channel assays

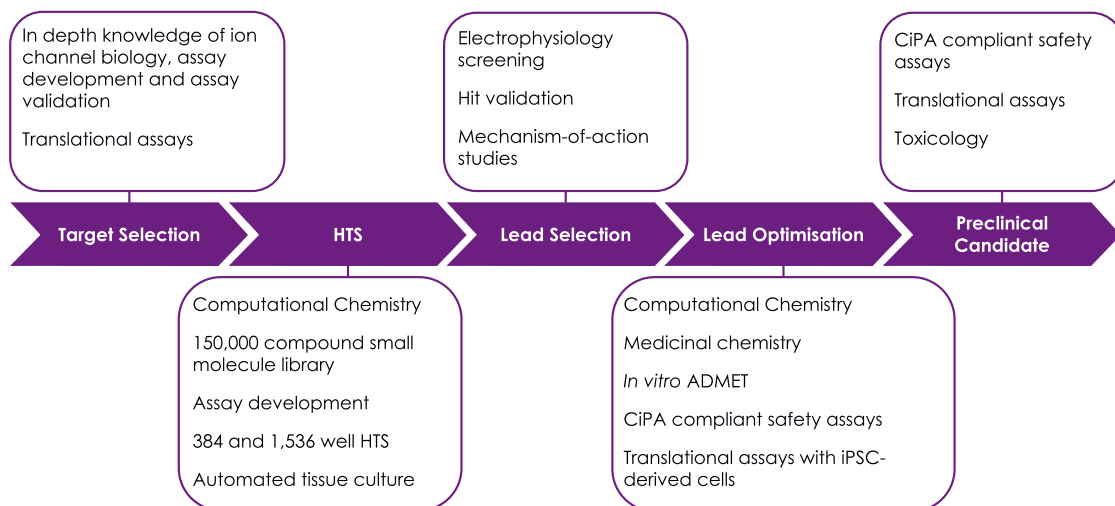
Assays designed and validated to meet your discovery research objectives

Speak to one of our team of experts to discuss your requirements

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# The Ion Channel Specialists Integrated Drug Discovery



Integrated drug discovery via Metribiosciences and our partners

info@metribiosciences.com      Tel: +44 (0) 1223 919 100      www.metribiosciences.com




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