NEWS RELEASE

Metrion Biosciences and International Scientific Consortium publish data and new recommendations for *in vitro* risk assessment of the cardiac safety of new medicines

Part of the US FDA's Comprehensive in vitro Proarrythmia Assay (CiPA) Initiative

Cambridge, UK, 07 April 2020: Metrion Biosciences Limited (Metrion), the specialist ion channel CRO and drug discovery company, today announced it has contributed to two new peer-reviewed papers under the U.S. Food and Drug Administration's (FDA) CiPA (Comprehensive *in vitro* Proarrhythmia Assay) initiative. The papers, in Nature Scientific Reports[1] and Toxicology and Applied Pharmacology[2], focus on application of improved cardiac safety testing protocols and recommendations for best practice for the drug discovery industry.

The CiPA Initiative (www.cipaproject.org), which began in July 2013 following a workshop at the US FDA, has the objective to revise and enhance the regulatory framework assessing cardiac safety of new chemical entities. Under current guidelines, new therapeutics undergo initial assessment of proarrhythmic risk by measuring activity against the hERG cardiac ion channel, before progressing to studies in preclinical animal models and ultimately, a Thorough QT interval study in the clinic. The CiPA initiative aims to extend the use of advances in early electrophysiology-based cardiac ion channel screening, *in silico* predictive modelling, and human induced pluripotent stem cell derived cardiomyocytes to improve the accuracy and reduce the cost of predicting the cardiac liability of new drug candidates. Metrion's research forms part of the first stage of the proposed harmonisation work, to provide clarity on how to standardise cardiac ion channel assays to ensure they deliver consistent data for *in silico* models of clinical cardiac arrythmia risk.

The first paper[1], published in Nature Scientific Reports on 27th March 2020 by an international group of authors drawn from 20 different commercial and academic laboratories, including Metrion Biosciences, was coordinated by the Health and Environmental Sciences Institute (HESI). It reviews data from a multi-year, multi-site collaboration across industry, academia and the FDA regulatory agency to optimize experimental protocols and reduce experimental variability and bias. The goal of the study was to guide the development of best practices for the use of automated patch clamp technologies in early cardiac safety screening. High quality *in vitro* cardiac ion channel data is required for accurate and reliable characterisation of the risk of delayed repolarisation and proarrhythmia in the human heart and to guide subsequent clinical studies and regulatory submissions.

The second paper[2], to be published formally in Toxicology and Applied Pharmacology paper on 1st May 2020 but currently available online, uses automated patch clamp data from the CiPA consortium to address the lack of statistical quantification of variability, which hinders

the use of primary hERG potency data to predict cardiac arrhythmia. The consortium establishes a more systematic approach to estimate *hERG* block potency and safety margins.

Dr Marc Rogers, CSO, Metrion Biosciences, said: *"The Metrion team has been a participant in the international CiPA Initiative since inception and we are now pleased to be able to announce the publication of our data from this global collaborative scientific effort. We believe these projects will make a significant contribution to the eventual revision of cardiac safety testing guidelines by the FDA and other international regulatory agencies. They also contribute to deepening our knowledge of the underlying causes of proarrhythmia, which will help prevent early attrition of potentially promising drugs."*

Contributing organisations to the Nature Scientific Reports CiPA study include: Charles River Laboratories; Bayer AG; Sophion Bioscience A/S; Nanion Technologies; GlaxoSmithKline PLC; Pfizer; Sanofi R&D; Astra Zeneca; B'SYS GmbH; Bristol-Myers Squibb Company; Eurofins Discovery; Merck; Metrion Biosciences Ltd.; Natural and Medical Science Institute at the University of Tübingen; Northwestern Feinberg School of Medicine, Chicago; Roche Innovation Center Basel; Novoheart; Health and Environmental Sciences Institute, Washington, DC; AbbVie.

Contributing organisations to the Toxicology and Applied Pharmacology hERG study include: Center for Drug Evaluation and Research, Food and Drug Administration; Eli Lilly and Company; AstraZeneca; CiPA LAB; NMI-TT GmbH; Sophion Bioscience A/S; B'SYS GmbH; The Ion Channel Company; F. Hoffmann-La Roche AG; Eurofins Discovery; Bristol-Myers Squibb; Merck & Co., Inc; Metrion Biosciences Ltd.; Nanion Technologies; Charles River Laboratories; Bayer AG; University of Nottingham; Université de Lille.

1. Cross-site and cross-platform variability of automated patch clamp assessments of drug effects on human cardiac currents in recombinant cells, Nature Scientific Reports

2. A systematic strategy for estimating hERG block potency and its implications in a new cardiac safety paradigm, Toxicology and Applied Pharmacology

For more information on Metrion's fully integrated Cardiac Safety Screening / CiPA Screening service, please visit: https://www.metrionbiosciences.com/services/cardiac-safety-screening/

Merion Biosciences' comprehensive cardiac safety testing 'White Paper' "**The changing landscape of cardiac safety**" will also be available on the Company's website from 13th April 2020.

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Notes to Editors

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About Metrion Biosciences www.metrionbiosciences.com
Metrion Biosciences is a specialist ion-channel contract research organisation and drug discovery business. The Company provides customers with access to a range of high quality ion channel assays on a fee-for-service or collaboration basis. Metrion Biosciences' ion channel expertise includes an industry leading panel of *in vitro* cardiac ion channel safety assays, translational native cell and phenotypic assays for neurological and cardiotoxicity testing, and a range of other ion channel screening services such as cell line development and optimisation. Metrion Biosciences is able to provide tailored assay formats, data analysis and reporting solutions, effective project management and quality assured data packages.

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