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INNOVATION IN MIND

Issue 4 - November 2016

Dear Shareholder,

Since our last newsletter published in April Medibio hit a key milestone with the first validation of its technology for the diagnosis of depression using independent clinical data from the University of Ottawa. As announced early August, we achieved an 83% accuracy rate in classifying individuals with major depressive disorder (MDD) from non-depressed individuals. This result, generated from a statistically significant clinical data set of 300 patients, underpins our confidence in our technology. But, more importantly, it cements our claim for commercial potential as a medical diagnostic tool.

While there were a couple of key differences between the Ottawa study and a clinical trial, there was significant equivalency. The first difference was the data set was retrospective. However, the data set and its collection parameters were the same as we're looking to capture in a clinical trial, such as our study with Johns Hopkins. The other difference was the Company analysed the clinical data set. In a clinical trial, an independent Research Organisation would perform the analysis with the trial blinded, the Company only receiving results at completion. However, an algorithm is not influenced by being blinded or unblinded.

Discounting the retrospective nature of the clinical data set, we have a pretty fair guide to the outcome we may expect from our **US clinical trial scheduled to be completed by the end of this year.** That trial will follow the completion of the Pilot Phase from the John Hopkins University (US) validation study of the Company's depression test this month.

Moreover, as highlighted in the August 8 announcement, our technology (essentially, a data crunching algorithm and its mechanism of action) evolves with iterations. That means it refines its accuracy as it processes greater amounts of data. The process is called advanced machine learning and its inherent in the software design. We, therefore, anticipate greater accuracy by the time it's used in the proposed clinical trial.

Additionally, other biomarkers the Company discovered in its sleep staging analytical study are anticipated to enhance the ability to assess depression (and other mental states).

Medibio's team is genuinely excited about the next several months. We hope you'll share in our enthusiasm.

Yours faithfully,

Kris Knauer
Chief Executive Officer (CEO)

Medibio breaks new ground in sleep analysis

Validated by the analysis of more than 13,000 hours of ECG files provided by one of MEB's collaborative research partners, John Hopkins University, Medibio's new sleep staging algorithm distinguishes the sleep stages to accuracies of 86-95%. This compares with the best previously published results in the 70% range.

Our existing algorithms for mental health will improve by incorporating new analytical metrics specific to sleep stages. Additionally, the ability to distinguish between sleep stages with greater accuracy using only ECG data has commercial potential in its own right.

Medibio redefines mental health by making the intangible, tangible.

Commercial importance of our technology

Skeptics may well ask: "Aren't psychiatrists already diagnosing depression adequately? Why would they want to use Medibio's test?"

The clinical 'gold standard' is a psychiatric diagnosis and the concordance of depression diagnosis among experienced psychiatrists is 70%[1]. Every 3 out of 10 patients referred to a psychiatrist is misdiagnosed.

In one notable study, US clinicians diagnosed some individuals of the same patient group as schizophrenia where as a separate diagnosis of the same group by UK counterparties labelled those individuals as schizophrenic. Again[3] why does this matter? Because the treatment of the specific disorder depends heavily on the initial classification.

At the primary care level (the US GP equivalent), the statistics are much worse with the accuracy of depression diagnosis 33-50%[2]. In other words, a misdiagnosis rate greater than 50%! It's no wonder depression is ranked one of the greatest health threats in the western world.

The problem Medibio's product aims to counter is this very subjective diagnosis of depression. It's done by patient survey, self-report and clinician observation and interpretation.

Whereas psychiatrists may be slow adopters of Medibio's depression diagnostic once it gains regulatory approval, the Company sees the front line general practitioners as its multiples-larger target market. GP's in Australia and the US are responsible for more than half of all mental health diagnoses.

There's sufficient press about the widespread prescription of anti-depressants with claims of over prescription and numerous accounts of side effects and serious adverse events. We see a future when Medibio's test, with a patient presenting to a GP or hospital emergency room, enable an objective, accurate diagnosis of suspected depression. Maybe one or two out of ten may be misdiagnosed using Medibio's technology. That's at first pass! Should the patient be diagnosed incorrectly or the test result's ambiguous, a follow-up can be performed readily should symptoms persist. Importantly, the misdiagnosis rate is dramatically lowered, enabling better patient outcomes.

Of no less important benefit is the ability to monitor a patient's treatment programme to determine an intervention's effectiveness. Not all medications act uniformly on people. Instead of a patient needlessly and, worse, harmfully, taking an ineffective medication, the physician can monitor a medication's effect objectively instead of waiting for latent signs of significant improvement.

Regulatory Approval

You may say that commercialisation depends on US FDA regulatory approval which the Company anticipates for 2018. What about the Company's fortunes in the meantime?

As well as stress, which we will touch on later, there are medical markets other than the US the Company plans to pursue. And, this is where the Ottawa data may pay off earlier.

Diagnostic software is classed as a medical device.

Medibio's technology for assessing mental health states is not a physical device but mathematical algorithms that analyse biological data collected by other approved heart rate monitors. As it pertains to diagnosing a clinical condition, regulatory authorities classify such algorithms as a particular medical device class. This is a much simpler regulatory pathway than a drug which requires Phase I, II and Phase III trials.

In the US, Medbio's depression test will be required to show its efficacy and safety in a clinical trial sanctioned by the FDA before granted marketing approval.

However, in the EU as well as Australia, the regulators may not require a clinical trial for marketing approval for certain medical devices.

The European Medical Devices Directorate (EMDD) mandates a device prove the scientific validity of its claims to acquire a CE Mark. A CE Mark allows the sale of medical device in the EU. Australia's Therapeutic Goods Administrator has likewise marketing approval domestically.

A Notified Body in the EU grants a CE Mark for medical devices and, when the device includes software coding, following an audit by an EU Certified Body. In Australia, the TGA performs the software code auditing.

The Company has started exploring its options for CE Marking for the European market including approval pathway, required validation studies, timeline, and budget for the process.

The Company seeks to discover whether the validation studies on the total retrospective data set when completed this year suffices for scientific validation under EMDD regulation. We anticipate having an expert opinion by the year's end.

There are two keys to commercialisation:

- **Sufficient clinical data (demonstrating good reliability, validity) and education. This relies primarily on *quality research* done by leading universities and Key Opinion Leaders.**
- **Insurance coverage or reimbursement after the requisite *FDA approval*.**

Stress the second string to our bow

Medibio's corporate stress product is also undergoing independent validation. The product, based on the Company's proprietary Digital Mental Health Platform (DMHP) for objectively classifying stress levels, forms the stress test component of its Mental Wellness solution package. Untreated chronic stress can result in serious health conditions including anxiety, insomnia, muscle pain, high blood pressure and a weakened immune system.

Contributing to the development of major illnesses, such as heart disease, stroke, depression, obesity and the potential spread of an individual's cancer via the lymphatic system.

Workplace stress is responsible for an estimated:

- 60% of workplace accidents,
- 30% of short and long term disability, and
- 40% of staff turnover.

In the US alone, stress costs employers an estimated $300 billion each year.

Notwithstanding the excellent results we've got to date, considerable success in the workplace wellness market and progress made on its improving deliverability to the end user (via coupling with wearables such as the *Applewatch* and *Fitbit Surge),* the Company realizes independent validation is needed to exploit the DMHP's full commercial potential.

Success in first Commercial Pilot Study

Medibio's first pilot study successfully demonstrated one of the core competencies of Medibio's objective Workplace Stress Test. The ability to identify "at-risk" employees where the traditional subjective measures often fail due to misleading self-reports used in conventional psychological assessment. Overall in the 5-week study of 66 employees of an Australian corporate, Medibio's Workplace Stress Assessment achieved 86% agreement with the conventional psych screening but, importantly, caught 2 at-risk employees who'd slipped through the net but were actually at the high-end of the stress scale. The study highlighted the need for Medibio's objective stress test to overcome the inherent deficiency of the conventional subjectively based assessments.

University Partnerships

As recently announced, Medbio partnered with the University of Sydney's Brain Mind Centre (BMC) to this end. Headed by Professor Nicholas Glozier, the BMC has taken over the supervision and data analysis of an existing trial comprising about 150 subjects which we hope will fast track independent validation.

The study's primary aim is to investigate the potential relationship between an individual's mood and stress levels and Circadian Heart Rate (CHR) patterns. The study will also investigate if symptoms of anxiety and depression are associated with distinctive pattern deviations in CHR.

The Company believes independent validation of its Mental Wellness solution by a leading academic institution will open significant markets beyond the workplace wellness market.

Expanded market opportunities include public services, health insurance providers, the military, aviation and the public health system where the Company believes independent validation is a prerequisite for widespread take-up of its Mental Wellness product.

MONASH University

Hot on the heels of this Medibio cemented a partnership with the Monash Institute of Cognitive and Clinical Neurosciences. The partnership aims to create innovative approaches to improve sleep and mental health outcomes in the general population by bringing together Monash University's world-leading sleep and circadian expertise and Medibio's mental health diagnostics capabilities.

The Monash Institute of Cognitive and Clinical Sciences is the largest Institute of its type in the Asia Pacific region, uniting over 200 world-class researchers with cutting-edge research infrastructure. The Institute is dedicated to understanding the brain and mind in key integrated research programs covering attention and memory, sleep, and addiction, and seeking to directly and actively support the use of this knowledge in the clinic, workplace, and also through collaborations with industry and the community.

The Medibio-Monash partnership will involve a broad range of initiatives focused on the further development of Medibio's early detection and monitoring solutions and Monash's advanced research and treatment approaches for sleep and circadian disorders for the clinical and work setting.

We hope the collaboration will translate cutting-edge science into next-generation mental health solutions. Monash share this view with Director of MICCN's Sleep Program, Professor Shantha Rajaratnam, saying:

"This collaboration with Medibio is an exciting and significant strategic step for MICCN as we look to translate our research into real-world outcomes through deep and enduring partnerships with industry".

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Australia's biggest mental health check-in

Finally, I would like to touch on a joint initiative of HBF, Vital Conversations and Medibio.

In partnership, we launched Australia's Biggest Mental Health Check-in campaign encouraging Australians to undertake a mental health check facilitated by Vital Conversations utilising Medibio's supplied device and technology. HBF will encourage its corporate clients to participate in the initiative. The campaign should result in a significant workplace trial of Medibio's diagnostic methodology.

The launch coincided with World Mental Health Day, the beginning of Mental Health Week in Western Australia and other mental health awareness programmes across Australia during October.

Supported by several high profile ambassadors, the programme aims to bring mental health and the benefits of stress screening into focus. The check-in aims to test 3,000 people using traditional self-report measures and Medibio's objective stress measure.

As well as the awareness created for our workplace stress product prior to commercial launch, other real benefits will be the expected 3,000 new de-identified data files with corresponding stress assessments. This data will more than quadruple the size of Medibio's dedicated overnight CHR file database and corresponding stress assessments.

Medibio shareholders are invited to participate for half price. This $26 cost includes your heart rate monitor and Medibio Stress App. Register on the checkin website at www.mentalhealthcheckin.com and enter the coupon code AMHC16MEB

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References

(1) *DSM-IV mood disorders field trial.* Keller et al : Am J Psychiatry 1995 Jun

(2) Trangle M, et al. Institute for Clinical Systems Improvement. Adult Depression in Primary Care. Updated March 2016

(3) The diagnosis and psychopathology of schizophrenia in New York and London.- US-United Kingdom Cross-National Project