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To: Parliament of Canada
Brief Submitted to the Standing Committee on Finance

A Healthy Population Ensures Economic Prosperity

Development of a Mental Health Diagnostic Tool (schizophrenia, bipolar disorders, major depression and anxiety)

A Canadian “Architectural Innovation” in Response to a Global Problem

The knowledge economy, innovation and entrepreneurship are strong drivers of growth and economic prosperity, when properly combined. Likewise, people will be more productive when they are healthy. Health care is a key sector for economic development (in Canada and globally) and is a fundamental value for Canadians. Mental and neurological health care has become a global priority, as mental disorders affect nearly 450 million people, according to the World Health Organization (WHO). About 20% of the global population is directly or indirectly affected. In Canada, the various mental disorders have a major impact on business productivity because of their extent and the cost of care. In 2012, the total estimated cost of mental health issues in Canada was $50 billion; it was $300 billion in the US, including $193 billion in lost earnings. Schizophrenia (SZ) alone affects 1% of Canada’s population, or 360,000 people, bipolar disorders (BP) touch another 1% and major depression (MD) afflicts 5%, or 1.8 million people. Together, these three diseases affected 22,558,760 people in the US in 2015. In Canada, the workplace impacts of mental disorders cost $16 billion, or 14% of Canadian businesses’ net annual profits. The direct consequences for family and loved ones must also be taken into account. In Canada, mental health is the second leading cause of hospitalization among individuals aged 15 to 34 and the third leading cause among those aged 35 to 44, all diseases considered. The indicators for these illnesses and their effects are constantly rising.

The lack of mental health diagnostic tools around the world

There is currently no test or biological measurement tool that can be used to establish a clinical diagnosis of SZ, BP or MD. Of the biomarkers reported in the neuropsychiatry literature, none satisfies the performance criteria of predictive value, non-invasive technique, ease of use and low cost, which greatly limits their use in medical practice, where interventions must be repeated periodically in keeping with the frequency of disease phases or cycles. Health professionals (generalists and psychiatrists) must therefore limit themselves to observing clinical symptoms and signs using various reference tools (e.g. the DSM-V). This poses many challenges and some risk of error. Between 30% and 40% of patients who suffer from SZ or BP have their diagnosis changed within the first

3 to 5 years of their illness; this figure increases to 40% to 50% for the first 7 to 8 years.

A number of factors can affect health professionals' decisions. Mental disorders are heterogeneous, the severity of symptoms varies and some aspects of them are shared with other illnesses, as is the case with SZ, BP and MD. Time is needed to evaluate the situation and make a differential diagnosis. Making the right diagnosis can take 6 to 30 months. Moreover, psychotic disorders can be induced by or confused with other conditions, such as substance abuse.

The estimated value of the market for a mental health diagnostic tool in Canada and the US is $3 billion. The first tool developed by diaMentis inc. is targeted at differential diagnosis of SZ and BP. We believe this tool will reduce the level of uncertainty (quantitative data and probability) and accelerate and improve the decision-making process given indications where the disease cycle is spread over several years. In short, the tool will save time, help confirm and clarify diagnoses and ensure the right problem is treated.

The tool's scientific basis

- There are many etiological factors (origins or causes) for mental disorders, and they differ from patient to patient. They may be genetic, environmental, psychological or social in nature or relate to neurobiological disturbances or neurotransmitter modulations (differences in certain regions of the brain or in neurotransmitter functions).
- During embryonic development, the eyes develop as an extension of the forebrain. The retina of the eye is composed of numerous neurons and is an extension of the central nervous system, which makes it an appropriate investigation site for evaluating certain anomalies.
- The results obtained from an examination of the retina (electroretinography, or ERG) in patients with SZ, BP and MD revealed different biosignatures, confirming the potential of this approach for producing a diagnostic tool to better manage these patients. The ERG test is simple, non-invasive and affordable, and it allows for measuring various parameters quantitatively. The data is interpreted through the use of algorithms developed from our database (which is intellectual property under the Patent Cooperation Treaty (PCT)).

Initial proof of concept, previous work in a university setting

The initial proof of concept is based on work performed between 2011 and 2014 by the team of doctors Michel Maziade, Chantal Mérette and Marc Hébert of Laval University's Centre de recherche de l'Institut universitaire en santé mentale de Québec (CRIUSMQ). This work and the retina exams conducted utilizing a

non-invasive technology used in ophthalmology for over 45 years enabled nearly 1,000 SZ, BP or MD patients and control subjects to be assessed.

A patent application (for North America and Europe) was filed on the basis of this work (see *PCT/CA2014/050233: Use of electroretinography (ERG) for the assessment of psychiatric disorders*).

The CRIUSMQ's data led to the following:

- the identification of specific biosignatures among SZ, BP and MD patients compared with normal subjects;
- the identification of biosignatures that could help make differential diagnoses of SZ, BP and MD; and
- the identification of biosignatures that could allow for stratifying SZ patients according to their response to treatments.

Initial partners

The initial work was made possible by funding from the Conseil québécois du développement du médicament (CQDM) and the Canadian Institutes of Health Research (CIHR). Currently, the development and commercialization stages are being conducted in an industrial setting by diaMentis inc. The initial work was also supported by Laval University's development and commercialization company, SOVAR. DiaMentis is made up of multidisciplinary experts in the life sciences. The investments required to commercialize the first tool are an estimated $10 million over a period of three to four years for the first indication (differential diagnosis of SZ and BP).

Current situation and development of first product

DiaMentis raised dilutive capital from private investors chosen for their leading-edge expertise in project-related areas. The National Research Council (NRC) provided a 12-month, non-repayable contribution of $350,000 for an initial $1.1-million project on May 31, 2016. We are convinced that the various levels of government—like our private investors—are highly interested in providing as much support as possible for the development of this diagnostic tool, which could significantly improve the management of mental disorders and the quality of life of those who live with them (first line and second line). Moreover, the benefits of reduced health care costs and the positive impact on families and caregivers are worth noting.

Very serious challenges to spinning off an innovative business

Like many other Canadian companies operating in the medical and diagnostic instruments sector, our business faces various challenges, including:

1. completing technical feasibility and development work on an effective and robust system in accordance with health agency compliance standards (Health Canada, the Food and Drug Administration (FDA), and the European Medicines Agency (EMEA));
2. completing validation studies for the first tool according to the expected conditions of use. Various collaborations must be arranged over the next three years with Canadian research centres and university hospitals (in Montreal, Ottawa and Toronto) and elsewhere in Canada for validation work, and more collaborations for validation studies must take place in the US (about 10 centres) and possibly in Europe; and
3. obtaining approvals and commercializing the diagnostic tool, and ensuring the first product is commercialized in a way that gives it the best chance of success on the global market.

We will provide a Canadian solution to a global problem while developing a business with cutting-edge industrial expertise (a unique competitive advantage) and attempting to keep the business's ownership balanced and ensure the value of the company (capitalization) is adequate relative to the funds required (rapidly raise enough new capital to fund new product development).

Preparation of new partnerships for commercialization on global markets

We hope to commercialize the entire platform (and a first product successfully) while developing a flagship Canadian business. Consequently, non-dilutive (repayable contribution) financing must be part of the funding arrangement. Yet, since 2002 this type of funding has been dropped from the Government of Canada's funding portfolio for innovative businesses. Given the scope and complexity of this project, partnerships must be developed to maximize the benefits for Canada, but with a business posture appropriate for a high-priority Canadian project. There is now a gap in this funding process for companies at our stage of development.

University commercialization companies, such as SOVAR, can corroborate this more specific problem.

All innovative businesses of this kind in Canada (high-technology university spin-offs) face the same challenges as we do. Access to repayable non-dilutive financing is therefore fundamental to advancing projects that are important to Canada's economy and the health of Canadians.

An innovative Canadian commercial solution to a global problem

The experts associated with the project (doctors and psychiatrists) are convinced of this platform's great potential based on the various results obtained to date. This new approach could therefore improve the management of patients with mental disorders. We believe that this will translate into better-quality care for all Canadians. In the medium run, the commercialization of other products using this platform will very likely reduce Canada's mental health care costs while increasing the services available for patients.

Canada's economic ecosystem is well-structured. However, some components that were once present in the (high-technology) innovation commercialization chain have disappeared. In a competitive global market, access to repayable non-dilutive capital is required to complete the next stages of feasibility and validation, for which the necessary studies will require major investments from 2017 to 2019. This kind of capital will help strengthen the business's structure by advancing the next stages of value creation. Even though the development cycle is short (four years), relatively inexpensive and less risky than it is for a pharmaceutical, the cost remains high for a business of our kind (a university spin-off with no revenue). Yet these investments are quite tiny compared with the business value (potential medical and psychological benefits) and the cost and impact of these diseases in the Canadian health care system. This non-dilutive financing will become marginal (if the product is successfully developed and commercialized), but no less fundamental for the growth of these businesses.