Shareholder Update on Cancer and Diabetes Programs

On December 16, 2014, we issued a press release updating the market on Nuvilex's cancer and diabetes programs. Please click here to view the press release: http://www.nuvilex.com/latest-news/147-nuvilex-provides-shareholder-update-on-cancer-and-diabetes-programs. To learn more about these programs, we have provided a comprehensive review below that includes the rationale behind our development strategy, the key members of the team and/or corporate partners who will advance these programs and, of course, milestones.

Pancreatic Cancer

Nuvilex holds the exclusive, worldwide rights to use the Cell-in-a-Box® cellulose-based live cell encapsulation technology for the development of a treatment for pancreatic cancer. Nuvilex is using its pancreatic cancer treatment (the combination of the Cell-in-a-Box® technology with low doses of the anticancer prodrug ifosfamide) in an attempt to combat pancreatic cancer on two fronts. On the basis of previous Phase 1/2 and Phase 2 clinical trials, this treatment has been shown to be safe and effective in patients with advanced, inoperable pancreatic cancer.

Effectiveness of Nuvilex's Treatment in Alleviating Symptoms Associated with Pancreatic Cancer and other Abdominal Cancers

Nuvilex is tackling the two major disease-associated symptoms that are suffered by patients with pancreatic cancer, namely the intractable and virtually untreatable pain and the accumulation of fluid (known as malignant ascites) in the abdomen that is extremely uncomfortable for patients with pancreatic cancer. Because this ascites fluid can contain cancer cells and these cells can seed and form new tumors, oncologists must remove ascites fluid on a regular and frequent basis. This is costly and painful.

The first preclinical study on the accumulation of ascites fluid has just been completed in the United States by Translational Drug Development (TD2), one of the premier Contract Research Organizations (CRO) in the U.S. that specializes in the development of cancer drugs and treatments. In this study, a mouse model system was used in which immunosuppressed mice were implanted with human ovarian tumor cells. These cells were chosen because they grow rapidly and produce significant amounts of ascites fluid.

After the tumor cells were implanted, the mice were divided into four groups: (i) a control group given only a "vehicle" control solution; (ii) a group given Nuvilex's pancreatic cancer treatment; (iii) a group given cisplatin, an effective anticancer drug against this type of tumor cells; and (iv) a group treated with the combination of Nuvilex's pancreatic cancer treatment plus cisplatin.

Although the data from this preclinical study have not been fully analyzed, upon initial review the results appear to be exceedingly positive and have now led to the design of a follow-up study. A final report will be forthcoming following the conclusion of the entire study.

Because there are no suitable animal models in which the effectiveness of Nuvilex's pancreatic cancer treatment can be determined in treating the very severe pain associated with pancreatic cancer, a human clinical trial will be necessary. This trial will be conducted by TD2 in the U.S.

In this trial the effectiveness of Nuvilex's treatment on pancreatic cancer-associated pain will be determined by following the quality-of life of patients with advanced pancreatic cancer and the extent of their use of analgesics to counteract the pain. Because this will be a human clinical trial, the Cell-in-a-Box® live cell encapsulation process must be done under Current Good Manufacturing Practices (cGMP) conditions. The completion of Austrianova's cGMP cell encapsulation facility in Thailand was a major and necessary step in preparing for this clinical trial.

Phase 2b Clinical Trial

Nuvilex is preparing to conduct a Phase 2b clinical trial in patients with advanced, inoperable pancreatic cancer. In this trial Nuvilex's pancreatic cancer treatment will be compared "head-to-head" with the current best available treatment for the disease. This treatment is the combination of gemcitabine [Gemzar®] with Celgene's drug Abraxane® (a nanoparticle albumin formation of the widely used cancer drug paclitaxel [Taxol®]). Such a comparison was not done in the previous two clinical trials that were completed in the early 2000s.

In those clinical trials, the results obtained with the Cell-in-a-Box® plus ifosfamide combination were compared to historical data for gemcitabine - the only drug approved at that time for use against pancreatic cancer. In addition, only two courses of administration of low-dose ifosfamide were used in the previous Phase 1/2 and Phase 2 clinical trials. For the Phase 2b trial, additional courses of ifosfamide will be administered in an effort to obtain even greater median survival time and percentage of one-year survivors than were seen in the previous trials.

Australia's leading CRO, Clinical Network Services (CNS), has been retained by Nuvilex to carry out the Phase 2b clinical trial in Australia. Through its past involvement with the Cell-in-a-Box® technology, CNS is familiar with Nuvilex's pancreatic cancer treatment. The "end-points" for the Phase 2b trial will include median survival time and percentage of one-year survivors, since these parameters are often determined in pancreatic cancer clinical trials. Like the previous Phase 1/2 and Phase 2 clinical trials, patients' quality-of-life will be assessed as they undergo treatment. Preparations for the clinical protocol (the recipe for conducting the clinical trial) are in progress.

European gastroenterologist/oncologist Dr. Matthias Löhr of the Karolinska Institute in Stockholm, Sweden, will play a major role in preparing for and conducting the Phase 2b trial. He is the ideal candidate for this role because he served as Principal Investigator for the previous Phase 1/2 and Phase 2 trials of the Cell-in-a-Box® technology and has developed an intimate knowledge of this technology and the use of Nuvilex's pancreatic cancer treatment in patients with advanced, inoperable pancreatic cancer. In addition, Dr. Löhr, Chairman of Nuvilex's Scientific Advisory Board, believes that this treatment will come to play a major role in the treatment of this devastating disease which he recently described as a "Medical Emergency" in an article published in the current (November) issue of The Parliament Magazine. Dr. Löhr's article can be found at https://www.theparliamentmagazine.eu/articles/magazines/celgene-making-difference-november-2014.

Nuvilex Australia will be handling every aspect of the Phase 2b clinical trial in Australia. With Nuvilex Australia conducting the Phase 2b clinical trial, Nuvilex will be in a position to take advantage of the Australian Government's Research and Development (R&D) Tax Incentive program which was established to encourage R&D development in Australia.

Orphan Drug Designation

The Orphan Drug designation is only given to drugs or treatments that are being developed to treat "rare" diseases. Because pancreatic cancer is considered one such disease by most countries, Nuvilex, with the

assistance of Dr. Matthias Löhr, Dr. Walter H. Günzburg, Dr. Brian Salmons, Dr. Gerald W. Crabtree, Dr. Natalie Thomas and personnel from CNS, has submitted applications to obtain orphan drug status to the EMA in Europe, the TGA in Australia and the FDA in the United States. The applications to the EMA, TGA, and FDA were sponsored by Nuvilex Europe, Nuvilex Australia and Nuvilex, respectively.

Orphan Drug status was previously granted by the EMEA (the EMA's predecessor) in the mid-2000s to Austrianova's predecessor for the Cell-in-a-Box® portion of what is now Nuvilex's pancreatic cancer treatment. If the orphan drug designation is granted by these drug regulatory authorities, the period of marketing exclusivity for Nuvilex's pancreatic cancer treatment can be extended by 10 years in the European Union, by 5 years in Australia and by 7 years in the United States.

Current Good Manufacturing Practices Live-Cell Encapsulation Facility

Nuvilex has contracted with its partner Austrianova to construct and equip a cGMP-compliant live cell encapsulation facility within the Thai Science Park in Bangkok, Thailand. This facility will be used for the Cell-in-a-Box® live cell encapsulation of the types of cells that will be required for clinical trials of Nuvilex's pancreatic cancer treatment as well as Nuvilex's future diabetes treatment.

In late November of this year, the construction of the facility was completed, and Nuvilex's Chief Executive Officer and Chief Operating Officer were privileged to attend its grand opening. In attendance were Thai government officials, principals from companies who had assisted Austrianova in the construction of the facility, officers and personnel from Austrianova and other invited guests. Approximately 50 people attended the grand opening. Pictures from the grand opening can be viewed on Nuvilex's website at: http://www.nuvilex.com/photo-gallery.

Now that the cGMP facility has been completed, several validation "runs" of the Cell-in-a-Box® live cell encapsulation process must be done. Once these have been completed, the cGMP facility will be inspected by the appropriate drug regulatory authorities to ensure that it, and the actual encapsulation procedures, comply fully with cGMP standards. After such inspections have been conducted and the facility is "approved" for use, the process will be initiated for the production of encapsulated cells for use in the various human clinical trials to be carried out by Nuvilex and Nuvilex Australia.

Diabetes

Over 380 million people have been diagnosed with diabetes worldwide, but approximately 185 million remain undiagnosed. Because the complications of diabetes (diseases of the eyes, kidneys, nerves of the feet and legs, and cardiovascular system) can be extremely serious and even deadly, it is imperative that effective treatments for the disease be developed.

There are two types of diabetes – Type 1 and Type 2. Type 1 (insulin-dependent or juvenile-onset diabetes) occurs because the insulin-producing beta islet cells of the pancreas have been destroyed by an autoimmune disease. In type 2 (adult-onset) diabetes, insulin is produced by the pancreas, but a phenomenon termed "insulin resistance" occurs whereby the available insulin is no longer of maximal effectiveness. Nuvilex plans to develop a treatment for Type 1 diabetes that is unique among available treatments for the disease. That treatment will also be available for those who need it and who have Type 2 diabetes where traditional medications are no longer effective.

Nuvilex's strategy is to develop a unique treatment for Type 1 diabetes involving the Cell-in-a-Box® cellulose-based encapsulation of human insulin-producing cells that are not of stem cell origin, nor are they pancreatic beta islet cells from human cadavers or from pigs.

Human Insulin-Producing, Non-pancreatic Cells

Nuvilex has obtained from the University of Technology Sydney (UTS) in Australia, the worldwide rights to use a line of insulin-producing cells developed by Prof. Ann Simpson and her colleagues at UTS for the development of a treatment for insulin-dependent diabetes. These cells, known as Melligen cells, originated from a human liver cancer cell line. They have been tested and shown to produce insulin in direct proportion to the amount of glucose in their surroundings, and a variety of other related studies have been done with them. Nuvilex's partners at Austrianova have successfully encapsulated these cells using the Cell-in-a-Box® technology. The cell line will soon undergo experiments at the University of Veterinary Medicine Vienna (UVMV) to see if they are suitable for use in Nuvilex's planned clinical trial to develop a breakthrough treatment for Type 1 diabetes.

The Nuvilex Diabetes Consortium

For some time now, it has been Nuvilex's intention to establish a Diabetes Consortium that consisted of world-renowned physicians and scientists from several countries, all of whom share the same goal of developing a treatment for insulin-dependent diabetes. In late November of this year, a meeting was held in Singapore at which the majority of individuals who make up the Diabetes Consortium were in attendance.

Participants in the meeting included Prof. Ann Simpson and Dr. Brenton Hamdorf of UTS. Dr. Eva Maria Brandtner of the Vorarlberg Institute of Vascular Investigation and Treatment in Austria also participated. Dr. Brandtner previously served as the Chief Scientist of Austrianova and while there performed preclinical studies with the Melligen cells developed by Prof. Ann Simpson. In addition, the meeting was attended by Dr. Constantine Konstantoulas of the UVMV and by Austrianova officers Dr. Walter H. Günzburg, Dr. Brian Salmons and Dr. John Dangerfield. Nuvilex's Chief Executive Officer, Kenneth L. Waggoner, and Chief Operating Officer, Dr. Gerald W. Crabtree, hosted and participated in the meeting. Dr. Matthias Löhr, as well as Drs. Eckhard Wolf and Rüdiger Wanke of the Ludwig-Maximillian University in Munich, Germany, were unable to attend due to previous commitments; however, all three were briefed by members of the Diabetes Consortium shortly after the meeting. The Nuvilex Diabetes Consortium has now been formed and is operational, with all participants actively engaged in projects that will lead to Nuvilex's planned treatment for insulin dependent diabetes. Pictures from the first meeting of the Diabetes Consortium held in Singapore on November 23, 2014, can be viewed on the Nuvilex website at: http://www.nuvilex.com/photo-gallery.

A Collaborative Research Agreement has been entered into between Nuvilex and the UVMV. It relates to a variety of preclinical studies that will be conducted by the UVMV that are needed for Nuvilex's diabetes program to be advanced. These preclinical studies will be conducted under the overall supervision of Dr. Walter H. Günzburg, a faculty member at the UVMV and Nuvilex's Chief Scientific Officer. Dr. Constantine Konstantoulas of the UVMV will be directing much of the research to be conducted at the UVMV. Several preclinical studies are being considered with the Melligen cells, all of which, if positive, should serve to considerably strengthen Nuvilex's position in the diabetes arena. Because the Melligen cells originated from a liver cancer cell line, these cells will be tested for their tumorigenicity (ability to form tumors). The tumorigenicity studies will be done in mice as well as some of the other preclinical studies to develop Nuvilex's treatment for diabetes.

A Collaborative Research Agreement is being negotiated between Nuvilex and the Ludwig-Maximillian University in Munich, Germany, to allow Nuvilex to use unique transgenic mouse and pig models of insulin-dependent diabetes. These model systems, developed by prominent scientists Dr. Eckhard Wolf and Dr. Rüdiger Wanke, will be used in the final stages of preclinical testing of Nuvilex's diabetes treatment that combines the Cell-in-a-Box® encapsulation technology with insulin-producing cells.

Dr. Löhr, who will assist Nuvilex in developing its Cell-in-a-Box® pancreatic cancer treatment, will also be actively involved as Nuvilex develops its treatment for insulin dependent diabetes.

Cannabinoids and Cancer

There are numerous examples of useful drugs that have been obtained or developed from plants. For example, the drug quinine, used for many years for the treatment of malaria, was first isolated from the *Cinchona* tree. The heart disease medication digoxin was derived from the compound digitalis found in the foxglove plant. Useful cancer drugs have also been isolated from plants. These include the vinca alkaloids, vincristine and vinblastine, isolated from the periwinkle plant. Taxol® (paclitaxel), first discovered in the bark of the Pacific yew tree, has come to be used for the treatment of a wide variety of cancers. Importantly, a derivative of paclitaxel known as Abraxane®, in combination with the cancer drug gemcitabine, is now the "gold standard" for the treatment of advanced, inoperable pancreatic cancer. In fact, the gemcitabine plus Abraxane® combination will be compared with Nuvilex's pancreatic cancer treatment in Nuvilex's Phase 2b clinical trial of this dreaded disease.

With the well-established history of deriving useful cancer drugs from plant sources, and in an effort to develop a "green" approach to the treatment of cancer, Nuvilex has embarked on a path of research that is designed to capitalize on the medicinal properties of components of *Cannabis* that are known as cannabinoids. *Cannabis* and its components have been used in medicine for centuries to treat a wide variety of ailments. Drugs developed from cannabinoids have been approved by drug regulatory authorities to treat medical conditions such as nausea, vomiting and pain for many years. More recently, the scientific literature has become replete with articles that testify to the activity of cannabinoids and cannabinoid-like compounds in the treatment of serious diseases, including cancer.

Nuvilex's initial plan is to combine the Cell-in-a-Box® encapsulation technology with cannabinoids or cannabinoid-like compounds to develop unique treatments for difficult-to-treat and deadly forms of cancer, such as brain cancer. As with Nuvilex's use of ifosfamide as the cancer prodrug that must be converted into its cancer-killing form, cannabinoid-based prodrugs will be used with the Cell-in-a-Box® technology in ways that optimize their anticancer properties while minimizing or even eliminating their adverse side effects long associated with chemotherapy.

The research being conducted by Dr. Richard M. Hyslop and other scientists at the University of Northern Colorado under a contract with Nuvilex is progressing well. Through the use of "model" cannabinoids, methods are being developed that will allow the separation and purification of various cannabinoids and cannabinoid-like compounds. In addition, efforts are underway to identify a type of cells that are capable of converting cannabinoid-based prodrugs into their cancer-killing form that will be encapsulated using the Cell-in-a-Box® technology. In the event that a suitable existing type of cell cannot be identified, one will be produced by Austrianova using genetic transformation as was done several years ago to create the cells for Nuvilex's Phase 2b pancreatic cancer treatment.

Most importantly, Nuvilex recently licensed from Austrianova the exclusive worldwide rights to use the Cell-in-a-Box® technology in combination with cannabinoid and cannabinoid compounds for the development of treatments for diseases and other medical conditions. Nuvilex's initial efforts to use the Cell-in-a-Box® technology with cannabinoids will be in the area of deadly and difficult-to-treat cancers, such as brain and pancreatic cancer.

Nuvilex has changed the name of its subsidiary Medical Marijuana Sciences, Inc. to Viridis Biotech, Inc. The word "viridis" in Latin means "green." This name change was made to not only emphasize Nuvilex's efforts in developing "green" disease treatments, but also to underscore that Nuvilex is not involved in the

growth, sales, or distribution of *Cannabis* or its various products and that Nuvilex is purely a biotech company developing treatments based upon cannabinoids or cannabinoid-like compounds for serious and deadly diseases around the globe.