

# MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Management's Discussion and Analysis of Financial Condition and Results of Operations ("MD&A") should be read in conjunction with the condensed unaudited interim consolidated financial statements of Helix BioPharma Corp. (the "Company" or "Helix") for the three-month periods ended October 31, 2017 and 2016 and the accompanying notes thereto. This MD&A is based on financial statements which have been prepared in accordance with International Financial Reporting Standards ("IFRS"). All amounts are depicted in Canadian currency unless otherwise noted.

Additional information relating to the Company can be found in the Company's Annual Information Form, which is available on SEDAR at [www.sedar.com](http://www.sedar.com).

## FORWARD-LOOKING INFORMATION

This MD&A contains forward-looking information (collectively, "forward-looking information") within the meaning of applicable Canadian securities laws. Forward-looking information means disclosure regarding possible events, conditions or financial performance that is based on assumptions about future economic conditions and courses of action and includes financial projections and estimates; statements regarding plans, goals, objectives, intentions and expectations with respect to the Company's future business, operations, research and development, including the focus of the Company on L-DOS47 which is the Company's primary drug candidate, Topical Interferon Alpha-2b and other information relating to future periods. Forward-looking information includes, without limitation, statements concerning (i) the Company's ability to continue to operate on a going concern basis being dependent mainly on obtaining additional financing; (ii) the Company's growth and future prospects being dependent mainly on the success of L-DOS47; (iii) the Company's priority continuing to be L-DOS47; (iv) the Company's development programs, including but not limited to, extension of the current drug candidate(s) to other indications and the identification and development of further tumour-targeting antibodies for DOS47; (v) the anticipated timeline for completion of enrolment and other matters relating to the Company's European Phase I/II clinical study for L-DOS47 in Poland, including the number of cohorts required to reach Maximum Tolerable Dose ("MTD") and the Company's U.S. Phase I clinical study for L-DOS47, (vi) seeking strategic partner support and therapeutic market opportunities; (vii) the nature, design and timing of future clinical trials (including the Company's anticipated reassessment of the re-design of the LDOS003 study to focus on advanced stage lung cancer patients by combining L-DOS47 with Vinorelbine/Cisplatin ("VIN/CIS") and commercialization plans; (viii) the Company's advancement in the area of cell based therapy via its subsidiary Helix Immuno-Oncology S.A. (formerly Helix Immuno-Oncology Sp. z.o.o. and Helix Polska Sp. z o.o.) ("HIO") (ix) future expenditures, insufficiency of the Company's current cash resources and the need for financing and the Company's possible response for such matters; (x) future financing requirements, the seeking of additional funding (including the possible receipt of grants) and anticipated future operating losses; (xi) changes in the application of accounting standards and interpretations; and (xii) industry performance, competition (including potential developments relating to immunotherapies and the Company's possible response to such developments), prospects, and general prevailing business and economic conditions. Forward-looking information can further be identified by the use of forward-looking terminology such as "expects", "plans", "designed to", "potential", "believe", "intended", "continues", "opportunities", "anticipated", "2017", "2020", "next", "ongoing", "seek", "objective", "estimate", "future", or the negative thereof or any other variations thereon or comparable terminology referring to future events or results, or that events or conditions "will", "may", "could", "would", or "should" occur or be achieved, or comparable terminology referring to future events or results.

Forward-looking information includes statements about the future and are inherently uncertain, and are necessarily based upon a number of estimates and assumptions that are also uncertain. Although the Company believes that the expectations reflected in such forward-looking information are reasonable, such statements involve risks and uncertainties, and undue reliance should not be placed on such statements. Forward-looking information, including financial outlooks, are intended to provide information about management's current plans and expectations regarding future operations, including without limitation, future financing requirements, and may not be appropriate for other purposes. The Company's actual results could differ materially from those anticipated in the forward-looking information contained in this MD&A as a result of numerous known and unknown risks and uncertainties, including, but not limited to:

- the Company's need for additional capital which may not be available in a timely manner or at all (whether from additional issuances of the Company's securities, grant applications or otherwise) and which, if not obtained, will have a material adverse impact on the Company and its ability to continue as a going concern;
- the risk that the Company may have to suspend or terminate one or more of its clinical trials for lack of funding, as the Company does not have sufficient funds to complete them and will need to raise additional funding, which is not assured;
- uncertainty as to whether the Company's drug product candidate(s), especially L-DOS47, will be successfully developed and marketed;
- developments in immunotherapies may result in significant changes in the treatment of cancer and may result in a reduction, which may be significant, in the potential patient population and/or treatment protocols available to chemotherapies and other treatments currently in development, such as the Company's primary drug product L-DOS47;
- the possibility of dilution to current shareholders from future equity financings;

- the impact of the ongoing volatility in the economic environment which has negatively affected the availability and terms of debt and equity financings and may have a negative effect on the Company's ability to raise further financing and its research and development initiatives;
- risk relating to the difficulty in enrolling patients in clinical trials which may result in delays or cancellation of clinical trials;
- intellectual property risks, including the possibility that patent applications may not result in issued patents, that issued patents may be circumvented or challenged and ultimately struck down, that any expiry of an issued patent, may negatively impact the further development or commercialization of the underlying technology, and that the Company may not be able to protect its trade secrets or other confidential proprietary information;
- research and development risks, including without limitation, the fact that the Company's drug product candidate(s) are complex compounds and the Company faces difficult challenges in connection with the manufacture of clinical batches, and the risk of obtaining negative findings or factors that may become apparent during the course of research or development, any of which may result in the delay or discontinuation of the research or development projects;
- partnership/strategic alliance risks and the need to secure new strategic relationships, which are both not assured;
- the Company's dependence on third parties, including without limitation, contract research organizations, contract manufacturing organizations, clinical trial consultants, collaborative research consultants, regulatory affairs advisors, and others, whose performance and interdependence can critically affect the Company's performance and the achievement of its milestones;
- the Company's dependence on assurances from third parties regarding licensing of proprietary technology owned by others, including the Company's dependence on its license of the L-DOS47 antibody;
- the need for future clinical trials, the occurrence and success of which cannot be assured, and the fact that results seen in earlier clinical trials may not be repeated in later trials;
- manufacturing risks, the need to manufacture to regulatory standards, uncertainty whether the manufacturing process for the Company's drug candidates can be further scaled-up successfully or at all and the risk that clinical batches of the Company's drug candidate may not be able to be produced in a timely manner or at all, which would have a negative effect on the timing and/or occurrence of planned clinical trials and the potential commercialization of the drug candidates;
- uncertainty as to the size and existence of a market opportunity for, and market acceptance of the Company's drug product candidate(s) including as a result of possible changes in the market for the Company's drug candidates resulting from development in immunotherapies or other future cancer treatments;
- uncertainty as to the availability of raw materials that the Company utilizes to manufacture its products, and in particular, Good Manufacturing Practice ("GMP") grade materials, on acceptable terms or at all, and that the Company may not be able to timely obtain alternative suppliers upon commercially viable terms or at all, which could have a material adverse effect on the further development and commercialization of any or all of the Company's drug product candidate(s);
- product liability and insurance risks;
- the risk of lawsuits and other legal proceedings against the Company;
- the effect of competition, especially from the new immunotherapy treatments for non-small cell lung cancer ("NSCLC");
- the risk of unknown side effects arising from the development, manufacture or use of the Company's products;
- uncertainty as to the Company's ability to maintain product liability insurance required by third parties and the risk of corresponding agreement being terminated;
- the risk of misconduct on the part of employees and consultants, including non-compliance with regulatory standards and requirements;
- the need to attract and retain key personnel and reliance on key personnel;
- that the Company has no sales, marketing and distribution experience;
- government regulation, including drug price regulation, and the need for regulatory approvals for both the development and profitable commercialization of products, which are not assured;
- risks associated with the fact that the U.S. Food and Drug Administration (the "FDA") and any other regulatory agency that the Company has consulted are not bound by their scientific advice, nor are any approvals given by one regulatory body binding on another;
- rapid technological change and competition from pharmaceutical companies, biotechnology companies and universities, which may make the Company's technology or products obsolete or uncompetitive;
- risks associated with claims, or potential claims, of infringement of third party intellectual property and other proprietary rights;
- the risk of unanticipated expenses;
- the impact on the Company's finances resulting from shifts in foreign exchange rates, credit risk and interest rate risk,
- risks relating to changes in the Company's tax rates;
- risk relating to a failure to maintain an effective system of internal controls;
- risks relating to the requirements of being a public company;

and other risk factors that are discussed above and elsewhere in this MD&A or identified in the Company's other public filings under the Company's profile on SEDAR at [www.sedar.com](http://www.sedar.com) (together the "Helix Risk Factors"), any of which could cause actual results to vary materially from current results or the Company's anticipated future results. Certain material factors, estimates or assumptions have been applied in making forward-looking information in this MD&A, including, but not limited to, the safety and efficacy of the Company's drug product candidate(s); the Company's cost and timing in connection with the Phase I U.S. clinical trial for L-DOS47; the cost and timing for achieving MTD in the Company's European Phase I/II clinical trial for L-DOS47 in Poland; that additional and sufficient financing will be obtained in a timely manner or at all to allow the Company to continue operations; the timely provision of services and supplies or other performance of contracts by third parties; future costs; the absence of any material changes in business strategy or plans, the timely receipt of required regulatory approvals, strategic partner support; and that the Helix Risk Factors will not cause the Company's actual results or events to differ materially from the forward-looking information.

For all of the reasons set forth above, which do not represent an exhaustive list of factors that may affect the forward-looking information, investors should not place undue reliance on forward looking information. The forward-looking information is based on the beliefs, assumptions, opinions and expectations of the Company's management at the time they are made, and the Company does not assume any obligation to update any forward-looking information should those beliefs, assumptions, opinions or expectations, or other circumstances change, except as required by law.

Data relevant to estimated market sizes in connection with Company's lead products under development are presented in this MD&A. These data have been obtained from a variety of published resources, including published scientific literature, websites and information generally available through publicized means. The Company attempts to source reference data from multiple sources whenever possible for confirmatory purposes. Although the Company believes the data is reliable, the Company has not independently verified the accuracy and completeness of this data.

## OVERVIEW

Helix is an immuno-oncology company primarily focused in cancer drug development. The Company is developing products for the treatment and prevention of cancer based on its proprietary technologies. The Company's product development initiatives are focused primarily on technologies that modulate the tumour microenvironment.

To date, the Company's proprietary technology platform, DOS47 has yielded two new drug product candidates, L-DOS47 and V-DOS47. L-DOS47 is currently under clinical study for the treatment of NSCLC. L-DOS47 has completed extensive preclinical testing and manufacturing development, following which, regulatory approvals to conduct a Phase I/II clinical trial in Poland and a Phase I study in the U.S. were obtained. V-DOS47 has been licensed to the Company's wholly owned Polish subsidiary for preclinical and clinical development. The V-DOS47 drug candidate uses the Company's proprietary DOS47 technology conjugated to anti-VEGFR2 antibody targeting a wide range of cancers.

The Company continues to actively pursue additional new antibody based technologies for cell-based therapies. In September 2016 the Company announced that it was developing a novel Chimeric Antigen Receptor T-Cell (CAR-T) therapeutic. The Company believes CEACAM6 specific CAR immune cells may have broad applications in a number of cancer types and is working on two camelid single domain antibodies that target CEACAM6.

The Company currently believes that its growth and future prospects are mainly dependent on the success of its DOS47 drug product candidates, and the successful development of cell-based therapies.

On December 23, 2016, the Company announced, it signed an exclusive out-license agreement with Xisle Pharma Ventures Trust ("Xisle") for the Company's late-stage, Biphasix™ technology platform, including the lead product candidate, interferon alpha. Xisle is responsible for the continued clinical development and subsequent commercialization of the product for the treatment of HPV-induced, low-grade, cervical intraepithelial lesions. As part of its asset development strategy, Xisle has initiated collaboration with senior pharmaceutical executives at Altum Pharmaceuticals Inc., who possess regulatory, clinical, and product development expertise. Under the terms of the agreement, Xisle paid an up-front fee of \$125,000 USD and agreed to pay subsequent milestone payments as they advance the technology to registration and market approvals and royalties. As part of the agreement, Helix retains marketing rights for Belarus, Bulgaria, Czech Republic, former Eastern Germany, Hungary, Moldova, Poland, Romania, Russia, Slovakia and Ukraine. In addition, the Company also retains non-exclusive rights for co-promotion in Canada.

The Company subsequently assigned the foregoing marketing rights which it retained to HIO, its wholly-owned subsidiary in Poland pursuant to an agreement between the Company and HIO with the agreement being subject to the restrictions and limitations associated with the out-license agreement signed between the Company and Xisle. In addition, HIO will be responsible for commercialization with milestone and royalty payments to be paid back to the Company upon successful product development through to commercialization.

The Company finances its research and development programs primarily from the issuance of its securities. In addition, the Company is also looking at alternative sources of additional financing. On July 21, 2016, the Company announced that its wholly-owned subsidiary in Poland had been awarded a funding grant from the Polish National Centre for Research and Development

("PNCRD") to develop V-DOS47. There can be no assurance that the Company will be successful in qualifying and/or receiving any additional grant money or that it will obtain additional financing or that the V-DOS47 program will be successful.

The Company expects to incur additional losses for the foreseeable future and will require additional financial resources to fund the Company's ongoing research and development activities and overhead costs.

The Company continues to not have sufficient cash reserves to meet anticipated cash needs for working capital and capital expenditures through the next twelve months. The Company's cash reserves as at July 31, 2017 of \$897,000 are not sufficient to see the current research and development initiatives through to completion or properly allocate scarce cash resources efficiently and as such, the Company will require additional financing in the very near term. Securing additional sufficient financing continues to be of critical importance to the Company.

Given the possibility of not being able to secure sufficient additional financing, whether on a timely basis or not at all, the Company may be required to reduce, delay or cancel one or more of its planned research and development initiatives, including clinical trials along with further reductions in overhead, any of which could impair the current and future value of the Company.

## **RESEARCH AND DEVELOPMENT ACTIVITIES**

### **Background**

The immune system utilizes two strategies in attacking different types of pathogens. The humoral immune system uses antibodies as its main weapon. Antibodies are proteins that bind to extracellular foreign invaders, such as bacteria, and lead to their destruction. The cellular immune system utilizes specialized immune cells, called T-cells to identify and bind to abnormal cells and subsequently destroy them.

Cancer cells have adopted and developed several strategies for evading the immune system. In some cases, proteins are expressed on the surface of tumour cells that "turn off" attacking T-cells. By using antibodies to block these interactions (such as anti-PD1), T-cells are reactivated to kill the tumours. Although anti-PD1 and anti-PDL1 therapies (checkpoint inhibitors) have improved outcomes for patients, there are many that do not respond to these treatments. One possible explanation suggests that the unique metabolism of cancer cells creates an acidic tumour microenvironment and this acidity has the effect of interfering with T-cell function. The Company believes it has developed a novel system to raise pH at the tumour site, thus breaking the physiologic barrier that acts to defend against tumour-killing T-cells.

### ***Alkalization using Urease***

Urease is an enzyme that catalyzes the hydrolysis of urea into carbon dioxide and ammonia ( $(\text{NH}_2)_2\text{CO} + \text{H}_2\text{O} \rightarrow \text{CO}_2 + 2\text{NH}_3$ ). The Company has conjugated urease to an antibody that specifically targets lung cancer cells, thus delivering the urease directly to the site of the tumour. L-DOS47, the Company's first drug product candidate, is currently in a phase I/II monotherapy trial in Poland and a Phase I combination trial with carboplatin and pemetrexed in the United States. By delivering urease to the tumour site, the company expects the pH of the tumour microenvironment to increase and activity of tumour-killing T-cells to be enhanced. The Company believes the urease system can be used with any tumour specific antibody as a general method for modifying the tumour microenvironment, and as such, could be combined with any of the current checkpoint inhibitor products to improve patient outcomes.

### ***CAR-T Cells***

To date, success in Adoptive Cell Transfer ("ACT") with engineered T-cells such as Chimeric Antigen Receptor T-cells ("CAR-T") has occurred mainly in the area of hematological malignancies. As of the end of 2016, 220 CAR T cell trials were documented of which approximately 188 are ongoing including nine long-term follow-up studies. Of the current trials, 133 target hematological malignancies and 78 solid tumors (Hartman et. al, EMBO Mol Med (2017) 9: 1183–1197). Most clinical trials have used autologous, unselected peripheral blood mononuclear cells ("PBMC") as the starting material and IL-2 for stimulation resulting in a CAR-T cell product consisting of CD4 and CD8 T cells with an activated effector T-cell phenotype. In five trials, more than 85% of treated patients reached complete response ("CR") as best clinical outcome (Hartman et. al, EMBO Mol Med (2017) 9: 1183–1197).

While CAR-T cell therapy has shown impressive clinical benefit, it is sometimes associated with a variety of toxicities that can be life-threatening. Several death cases have been reported, especially in the last year. These were due to neurotoxicity caused by cerebral edemas in the CD19-CAR trials sponsored by Juno Therapeutics. Whether neurological toxicities are solely restricted to CD19-specific CAR-T cells or generally associated with CAR-T cell therapy remains to be elucidated (Hartman et. al, EMBO Mol Med (2017) 9: 1183–1197).

A direct connection to another frequent side effect, the cytokine-release syndrome ("CRS"), also appears likely. CRS has so far been the most frequently observed adverse drug reaction. On-target, off-tumor recognition has become a relevant concern, since many targeted tumor antigens are also expressed on normal tissue (Hartman et. al, EMBO Mol Med (2017) 9: 1183–1197).

On August 30, 2017, the FDA approved Novartis' Kymriah (tisagenlecleucel) for certain pediatric and young adult patients with a form of acute lymphoblastic leukemia ("ALL"). Kymriah is a genetically-modified autologous T-cell immunotherapy. Each dose of Kymriah is a customized treatment created using an individual patient's own T-cells.

Solid tumours have created challenges and as such, it is hypothesized that the failure of CAR-T therapies to date may be the result of the acidic tumour microenvironment surrounding the cancer cell that inhibits CAR T-cell activity. The Company believes it is well positioned to use its proprietary urease-antibody technology to alkalinize the tumour microenvironment and improve the ability of CAR-T cells to destroy solid tumours.

### **Check Point Inhibitors**

Dr. Robert J. Gillies of the Moffitt Cancer Center in Tampa Florida demonstrated some interesting results when treating acidic tumours in animal models. Dr. Gillies demonstrated that in alkalinized tumour cells, the activity of antibodies that target PD-L1, is enhanced. This would indicate that tumour acidosis may protect tumours from immune check-point inhibitors. Since tumour acidosis is experimentally shown to occur in cancers such as breast, colon, lung and pancreas, the Company believes methodologies that can alkalinize the tumour microenvironment, such as the Company's proprietary DOS47 platform technology, may work beneficially with check-point inhibitors.

### **DOS47 – A broad anti-cancer therapeutic platform**

DOS47 is based upon a naturally occurring enzyme isolated from the jack-bean plant called urease that breaks down a natural substance found in the body, urea, into metabolites that include ammonia and hydroxyl ions. By doing so at the site of cancerous tissues in the body, the Company believes DOS47 can modify the micro environmental conditions of cancerous cells in a manner that leads to apoptosis.

DOS47 stimulates an increase in the pH of the microenvironment surrounding the cancerous cells, effectively reversing the acidic extra-cellular conditions that are believed to act to defend the tumour. This acidic environment can also reduce or negate the effectiveness of some commonly used anti-neoplastic agents. The local production of ammonia at the site of cancerous tissues is thought to readily diffuse into the cancer cells to exert a potent cytotoxic effect by interfering with their critical metabolic functions. Enzymatic action of urease at the site of cancerous cells is potentially repetitive and sustainable due to the plentiful supply of urea.

The Company is pursuing the development of DOS47 both as a monotherapy and as an adjunct therapy in combination with certain chemotherapeutics and/or radiation regimens, with a view to maximizing the DOS47 commercial potential.

DOS47 candidates are produced by conjugating urease with a targeting antibody or antibody fragment that can specifically direct the urease to the surface of a cancer cell. Once docked to the cell, the urease produces ammonia enzymatically through the conversion of urea found throughout the body. These conjugates of antibodies to urease are called DOS47 candidates. By selecting antibodies that are selective to different tumour cell surface receptors, the Company believes that DOS47 candidates can be used in several types of solid tumours.

In fiscal 2015, the Company entered into a collaborative research agreement with Affilic to assess proprietary anti-tumour targeting agents in combination with DOS47. The agreement calls for a feasibility study using a targeting agent in conjugation with DOS47. Continuing development of these new conjugates is subject to a successful feasibility study, execution of a formal development and licensing agreement, and the availability sufficient financial resources.

The Company continues to reach out to third parties in order to identify and test additional tumour-targeting antibodies for conjugation with DOS47. In the event that antibody candidates worthy of further development are identified, the Company will need to discuss development and licensing arrangements, which may not be available on terms acceptable to the Company or at all.

### **L-DOS47**

The Company believes that its DOS47 candidates may have potential anti-cancer activity by stimulating an increase in the pH of the microenvironment surrounding the cancerous cells. The local production of ammonia at the site of cancerous tissues is thought to readily diffuse into the cancer cells and may exert a potent cytotoxic effect by interfering with their critical metabolic functions. In addition, the Company believes that the use of DOS47 candidates may also have a synergistic effect on the efficacy of other marketed chemotherapeutics, such as vinka alkylid analogues, where low pH can inhibit the cellular uptake of these agents. The Company believes the enzymatic action of urease to increase the pH at the site of cancerous cells is repetitive and sustainable due to the plentiful supply of urea that is furnished by the body.

L-DOS47 is the Company's first targeted therapeutic immune-conjugate under development based on the DOS47 technology.

L-DOS47 is an antibody protein conjugate where the urease component enzymatically converts naturally occurring urea to ammonia. The L-DOS47 drug molecule includes a highly specialized camelid-derived single domain antibody, designed to identify a unique CEACAM6 antigenic site associated with NSCLC cells. By delivering the conjugate in a targeted manner, the Company

believes L-DOS47 stimulates an increase in the pH of the microenvironment surrounding the NSCLC cells, reversing the acidic extra-cellular conditions that are shown to be favourable for cancer cell survival.

L-DOS47 is intended to offer an innovative approach to the first-line treatment of inoperable, locally advanced, recurrent or metastatic NSCLC. However, other emerging therapies, including immunotherapy, may alter the treatment paradigm in NSCLC. Therefore, the eventual approval for L-DOS47 as a first-line treatment for NSCLC will depend on both successful clinical trials and on the treatment landscape shaped by these new therapies. The Company continues to monitor developments in this area and to consider their effect on its L-DOS47 program, including its focus on L-DOS47 as a first-line treatment for NSCLC.

In 2005, the Company entered into a worldwide exclusive license with the National Research Council of Canada ("NRC"), through which it obtained the rights to combine this highly specialized camelid-derived single domain antibody with Helix's DOS47 technology. As a result, the Company has certain royalty and milestone payment obligations pursuant to the license agreement. The license agreement with the NRC has been filed under the Company's profile on SEDAR at [www.sedar.com](http://www.sedar.com). The NRC filed patent applications in respect of the antibody in Canada, the United States and other countries. On March 2, 2011, the NRC was issued a U.S. patent in respect of the antibody.

In addition to being a key for cancer progression by promoting invasiveness and metastatic behaviors of cancer cells, the acidic tumour microenvironment protects cancer cells from immunotherapy by suppressing the proliferation and cytotoxic activities of local immune cells. The interactions of programmed cell death protein 1 (PD-1) on Jurkat cells with its ligand PD-L1 were studied. The human cancer cell lines MDA-MB231 and BxPC-3 were stimulated with Interferon gamma (IFN $\gamma$ ) to express PD-L1 on the cell surface. The IFN $\gamma$ -stimulated cell lines were found to inhibit IL-2 production in co-incubated Jurkat cells by as much as 40% when compared to non-stimulated cells. The addition of L-DOS47/urea to the culture medium partially restored cytokine production in Jurkat cells, suggesting a potential role of L-DOS47 in the process of PD-1/PD-L1 interactions.

On July 11 and 18, 2017, the Company announced that it had entered into a collaboration agreement with Moffitt Cancer Center to perform basic research studies to further investigate the pharmacodynamics of L-DOS47 and determine the potential benefits of combining L-DOS47 with immune checkpoint inhibitors. Under the research plan Moffitt Cancer Center will perform in vitro and in vivo research studies to study the pharmacodynamics of L-DOS47 and its effect when combined with check-point blockage agents using their unique tumor models.

#### **V-DOS47**

V-DOS47 is an antibody DOS47 conjugate that targets the vascular endothelial growth factor 2 receptor (VEGFR2). V-DOS47 is the second immuno-oncology drug candidate derived from the Company's DOS47 technology platform.

In January 2016, the Company granted a world-wide exclusive license for V-DOS47 to its wholly-owned subsidiary, HIO in Poland. The Company expects that day-to-day development activities in respect of V-DOS47 will be coordinated by HIO with coordination and oversight from some of the Company's scientists in Canada.

In order to advance the V-DOS47 initiative in Poland the Company is establishing a wet lab facility with the majority of the funding coming from the grant application with the PNCRD.

The Company had previously developed four V-DOS47 research candidates and conducted in vitro feasibility studies to establish the potential clinical applications for these molecules. HIO is expected to leverage this know-how to develop a V-DOS47 clinical drug product candidate. The Company will assist HIO by sharing its extensive knowledge in GMP manufacturing, preclinical research and clinical experiences. HIO will collaborate with several Polish institutes through the grant to complete the development of the first v-DOS47 clinical drug product candidate. The development of the clinical drug product candidate for Phase I testing is expected to take two to three years. The actual duration of the development process will depend on successful completion of preclinical research favorable for clinical testing and establishment of cGMP manufacturing processes. The Company expects to enter clinical trials in 2019 provided success is achieved during the preclinical and there are sufficient funds.

The Company is also leveraging its know-how in manipulating the tumour microenvironment, and its expertise in developing unique single domain antibody therapeutics to develop CAR-T novel cell based treatments. Helix intends to develop CARs for ACT for solid and hematological malignancies. The Company has selected CEACAM6 and VEGFR2 specific CARs for solid tumour. For hematological malignancies the Company has selected CD19 and CD22.

As announced by the Company in August of 2017, a peer-review of V-DOS47 was published in the "Frontiers in Immunology" journal. V-DOS47 is Helix's second DOS47 development candidate following L-DOS47, which is currently in clinical testing for the treatment of triple negative breast cancer. The article, entitled "Development and Characterization of a Camelid Single Domain Antibody-Urease Conjugate That Targets Vascular Endothelial Growth Factor Receptor 2", describes the design and construction of V-DOS47 for breast cancer and other potential indications.

## **CAR-T solid tumours**

### *CEACAM6 specific CARs*

Expression of CEACAM6 protein has been reported in a variety of normal human tissues including granulocytes. However, its expression is elevated in many types of solid tumours such as breast, pancreatic, ovarian, lung and colon. CEACAM6 is envisaged as a biomarker and potential therapy target for pancreatic ductal adenocarcinoma and pancreatic intraepithelial neoplasia (Duxbury et al., 2004a, 2004c, 2004d). Recently CEACAM6 is suggested to be check point molecule in multiple myeloma.

The Company believes CEACAM6 specific CAR immune cells may have broad applications in a number of cancer types. The Company is working on two camelid single domain antibodies that target CEACAM6.

2A3 is a camelid single domain antibody isolated from a whole cancer cell immunized llama library. The antibody binds specifically to the CEACAM6 antigen with high affinity and inhibits the proliferation of CEACAM6-expressing cancer cells *in vitro*. The efficacy of CEACAM6-CAR-T cells in xenograft model was examined *in vivo*. The results strongly support that CEACAM6-CAR-T cells can be used as an effective immunotherapy agent against CEACAM6-expressing cancers, and that camelid single domain antibodies can be easily adopted for CAR-T type therapies.

### *Vascular epithelial growth factor receptor 2 (VEGFR2) CARs*

Most solid tumours and some hematologic malignancies are characterized by an angiogenic phenotype that is an absolute requirement for tumour survival, progression, and metastasis. Therapeutic approaches targeting molecules involved in tumour angiogenesis can inhibit tumour growth. Proliferating endothelial cells in the vessels within solid tumours aberrantly express high levels of angiogenic growth factors, receptors, and adhesion molecules that are absent or barely detectable in established blood vessels, which are normally quiescent. Among these, VEGF and its receptors appear to be the dominant regulators of angiogenesis responsible for the vascularization of normal and neoplastic tissues. Overexpression of VEGF and its receptors is associated with tumour angiogenesis, survival, invasion, metastasis, recurrence, and prognosis in human cancers. VEGF stimulates angiogenesis mainly through VEGFR-2 (also known as Flk1 in mice and KDR in humans), a tyrosine kinase receptor that is overexpressed in tumour endothelial cells and on some tumour cells. Pharmacologic approaches to inhibit VEGF, using monoclonal antibodies or small molecules, are of value in cancer treatment, though the cytostatic rather than cytotoxic nature of these interventions and the redundancy of angiogenic pathways have limited the curative potential of these treatments). The Company believes VEGFR2 specific CAR immune cells may have broad applications in a number of cancer types. Helix is working on two camelid single domain antibodies that target VEGFR2.

The Company is also leveraging its know-how in manipulating the tumour microenvironment, and its expertise in developing unique single domain antibody therapeutics to develop CAR-T novel cell based treatments. Helix intends to develop CARs for ACT for solid and hematological malignancies. The Company has selected CEACAM6 and VEGFR2 specific CARs for solid tumour. For hematological malignancies the Company has selected CD19 and CD22.

The Company is also exploring opportunities for collaboration on complementary technologies to advance Company development in cell based immune-oncology therapies.

The Company has also approached five Polish hospitals with plans to establish centers of excellence (European Center for Cancer Immunotherapy ("ECCI")) that will participate in the development of their proprietary immune therapies. The Company will be seeking investment in the establishment of the ECCI in Poland once a business/strategic plan has been finalized and approved by the Company's Board of Directors.

## **Clinical study initiatives**

Regulatory approvals were granted to conduct a Phase I/II monotherapy (LDOS002) and a Phase I combination study (LDOS001) of L-DOS47 in Poland and the U.S. respectively, for the treatment of NSCLC. In addition, the Company plans to initiate study LDOS003, a clinical trial of L-DOS47 in combination with VIN/CIS in NSCLC patients with metastatic solid tumours.

### *U.S. Phase I clinical study ("LDOS001")*

On February 7, 2011, the Company announced it received approval by the FDA to conduct a U.S. Phase I clinical study with L-DOS47. The Company originally planned to commence the L-DOS47 U.S. Phase I study during fiscal 2012 but, given the Company's limited cash resources, the Company had prioritized the LDOS002 European Phase I/II clinical study with L-DOS47 in Poland while deferring the previously planned commencement of the U.S. Phase I clinical study with L-DOS47.

On April 22, 2014, the Company announced an IND approval by the FDA to commence a study for an L-DOS47 Phase I, open label, dose escalation study in combination with standard doublet therapy of pemetrexed/carboplatin in patients with Stage IV recurrent or metastatic non-squamous NSCLC. The Company has initiated three U.S. sites: Dr. Sarina Piha-Paul at the MD Anderson Cancer Center, Dr. Chandra Belani at Penn State University and the Milton S. Hershey Medical Center, and Dr. Afshin Dowlati at University Hospitals Case Medical Center.

Nine patients were successfully dosed at the first two L-DOS47 dose levels 0.59 and 0.78 µg/kg respectively.

On November 30, 2016 the Company announced that after reviewing safety data from the Phase I/II study of L-DOS47 in non-squamous non-small cell lung cancer (LDOS002), the FDA had accepted an accelerated escalation scheme for L-DOS47 dosing in the U.S. Phase I study (LDOS001) up to 12µg/kg in combination with pemetrexed/carboplatin.

The Company provided an update to the LDOS001 study at the Biotech Showcase meeting on January 10, 2017 in San Francisco. Highlights of the presentation included the following:

- No dose limiting toxicities reported at doses up to 0.78µg/kg;
- Partial responses were reported in three (3) of the first six (6) patients dosed;
- Best tumour response reported was a 44% reduction in the sum of target lesions measured; and
- Three (3) patients continued L-DOS47 monotherapy following induction therapy of L-DOS47 in combination with pemetrexed/carboplatin.

On May 26, 2017, the Penn State Cancer Institute (PSCI) the closure of the site due to limited enrollment activity. The site has subsequently been closed and no longer actively recruiting patients.

On June 29, 2017, the MD Anderson Electronic Protocol Accrual Auditing Committee (ePAAC) met to review the LDOS001 protocol due to slow patient recruitment. The committee decided to keep the protocol open for for an additional six months at which time, another review will be conducted.

On July 25, 2017 the Company announced the opening of patient screening in the third dosing cohort. After a review of safety data, the Safety Review Committee ("SRC") recommended that Helix begin enrollment of patients into the third dosing cohort of study LDOS001. Patients enrolled in the third dosing cohort will receive 1.50 micrograms of L-DOS47 per kilogram of patient body weight in combination with pemetrexed/carboplatin.

On September 27, 2017 the Company announced that the FDA had approved an amendment to their U.S. Phase I study, protocol LDOS001, accelerating the dose escalation phase of the study. In order to maximize the number of patients receiving a potentially active dose of L-DOS47, the study will implement an accelerated dose design up to 6µg/kg followed by a standard 3+3 design for the final two dosing cohorts, 9 and 12 µg/kg respectively.

To date, of the nine (9) patients in the LDOS001 study dosed to date, four (4) patients have had a confirmed partial response (as defined by RECIST v1.1) following treatment of L-DOS47 in combination with pemetrexed/carboplatin. Four (4) patients continued weekly L-DOS47 weekly maintenance therapy, of which two (2) were progression free for greater the one year after the initiation of treatment.

To address patient enrollment issues, the Company request a protocol amendment, which was approved by the FDA, to reduce the number of patients required to complete the study. Furthermore, in the next fiscal year, the Company plans to open additional sites.

The Company continues to have insufficient cash resources to see the entire LDOS001 U.S. Phase I clinical study through to completion. Given the Company's limited current cash resources and the possibility of not being able to obtain additional financing on a timely basis, the Company may be required to reduce, delay or cancel one or more of its planned research and development programs, including clinical trials along with further reductions in overhead, any of which could impair the current and future value of the business.

#### *European Phase I/II clinical study in Poland ("LDOS002")*

On July 25, 2011, Helix announced that the Company had received approval from the Central Register of Clinical Trials at the Polish Ministry of Health to perform a European Phase I/II clinical study with L-DOS47 and, on May 14, 2012, announced that clinical site initiation and patient recruitment activities had commenced for its European Phase I/II clinical study of L-DOS47. On October 23, 2012, the Company announced that its first patient had been enrolled and the first dose had been administered in this study.

The study is being conducted at five Polish centers under the direction of Dr. Dariusz Kowalski at The Maria Sklodowska-Curie Memorial Cancer Centre & Institute of Oncology as the overall coordinating investigator, together with four other principal investigators: Prof. Cezary Szczylik, MD, PhD at the Military Medical Institute, Prof. Elzbieta Wiatr, MD, PhD at the National Tuberculosis and Lung Diseases Research Institute, Dr. Aleksandra Szczensa, MD, PhD at the Mazovian Center of Pulmonary Diseases and Tuberculosis in Otwock and Prof. Rodryg Ramlau, MD, PhD at Med. Polonia Hospital Poznan.

The study is being conducted in patients with inoperable, locally advanced, recurrent or metastatic, non-squamous stage IIIb/IV NSCLC. The study, which is now well underway, recruits patients eligible for inclusion into escalating doses of L-DOS47 given



as a monotherapy. The study utilizes an open-label design, allowing for periodic status updates through its course. The study is intended to demonstrate valuable safety and proof-of-concept efficacy data for L-DOS47.

Patients in the study receive weekly doses of L-DOS47, administered as an intravenous infusion over 14 days, followed by seven days' rest (one treatment cycle is three weeks). Once the MTD of L-DOS47 has been determined in Phase I, an estimated 20 patients will be enrolled to evaluate the preliminary efficacy of L-DOS47 in the Phase II portion of the study.

Enrolment in the Phase I component of the study is now complete. A total of 55 male and female patients, at least 18 years of age, with histologically confirmed non-squamous NSCLC were dosed at 16 L-DOS47 dose levels. Patients have an Eastern Cooperative Oncology Group performance status of 0 – 2 at the screening visit for this study, and have at least one site of measurable disease per RECIST v1.1.

The Phase II component enrolls the same patient population as the Phase I at an L-DOS47 dose of 13.55µg/kg. Patients in the study are dosed twice weekly over 14 days (Days 1, 4, 8, 11) followed by a 7-day rest. To date, a total of 21 patients have been dosed in the first stage of the Phase II component of the study.

To date, the Company has completed four interim data reviews in connection with the LDOS002 study.

On October 15, 2013, the Company announced the completion of an interim data review of the first four cohorts for this study. The release stated that L-DOS47 was well tolerated for all patients treated within all cohorts. None of the treatment related adverse events reported to date has met the definition of a dose-limiting toxicity. Adverse events reported as of that date are those normally expected for the population under study.

A review of available pharmacokinetic ("PK") and immunogenicity data showed that these data so far, are consistent with trends seen within pre-clinical animal studies of L-DOS47. Results from these reviews, together with safety data will provide guidance on the treatment schedule and dosing for the Phase II portion of the study.

Based on Radiologic Evaluations, patients assigned a status of "Progressive Disease" following any such assessment were withdrawn from the study. At least one patient in each of the four cohorts dosed had a radiological assessment of "Stable Response". Duration of treatment increased with each dose escalation up to Cohort 4. One patient in Cohort 3 was dosed for 6 cycles without disease progression. None of the patients treated to date have had a partial or complete response as defined by RECIST v1.1 definition.

On September 30, 2014, the Company announced the completion of a further interim data review for the first eight cohorts for the LDOS002 study. The review included all available data, including patient demographics, safety assessments, PK data, immunogenicity and radiological tumour assessments. The following observations were made:

- adverse events reported are those expected for investigational product and population under study;
- no Dose Limiting Toxicities ("DLTs") have been reported;
- stable disease observed in radiological assessments of 12 of 24 (50%) of patients treated; and
- two patients completed six cycles of treatment each.

On September 8, 2015, the Company announced the presentation and update of the ongoing clinical study LDOS002 for the Company's drug candidate L-DOS47 during the 16th World Conference on Lung Cancer held in Denver Colorado. The presentation included the following data:

- 40 patients were enrolled in the first twelve dosing cohorts;
- L-DOS47 was well tolerated at the dose levels up to 4.33 µg/kg;
- No DLTs were reported for Cohorts 1-12;
- One (1) DLT was reported for Cohort 13;
- adverse events reported to date were expected for the population under study;
- 21 of the 40 patients had an overall response of stable disease based on radiological assessment after completing two cycles of L-DOS47;
- 11 of these 21 patients continued with a response of stable disease based on radiological assessment after completing four cycles of L-DOS47;
- one (1) patient in cohort 9 was dosed for 10 cycles (approximately seven (7) months) without disease progression;
- the study is currently enrolling patients in the thirteen-dosing cohort (5.76 µg/kg).

On December 6, 2016, the Company presented the following LDOS002 Phase I data for the Company's drug candidate L-DOS47 during the 17<sup>th</sup> World Conference on Lung Cancer held in Vienna, Austria:

- 90 patients were consented and screened for participation in the study;
- 55 patients were administered at least one dose of L-DOS47 at dose levels ranging from 0.12 to 13.55µg/kg;
- 21 patients completed four treatment cycles and 16 patients were administered additional L-DOS47 cycles;

- comparatively, patients in cohorts 13 to 16 (5.76 to 13.55µg/kg) were exposed to more L-DOS47 for a longer duration without a significant change to the safety profile of L-DOS47 compared to the other dosing cohorts;
- 44, or 80% of the patients in the safety population had at least one treatment emergent adverse events;
- L-DOS47 did not elicit a dose-dependent release of cytokines at doses up to 13.55µg/kg
- the MTD of L-DOS47 was not reached in the Phase I component of study LDOS002 at doses administered up to 13.55µg/kg;
- L-DOS47 was well tolerated at all dose levels up to 13.55µg/kg.
- a dose response trend was observed when comparing the percentage of patients who were progression free at 16 weeks across dose ranges;
- a similar trend was observed when comparing the percentage of patient who had an overall tumour response of Stable Disease (as defined in RECIST v1.1) and had a reduction in the sum of target lesions;
- 11 of 14 or 79% of patients in the highest dosing cohorts (5.76 to 13.55µg/kg) had an overall tumour response of Stable Disease following the administration of two cycles of L-DOS47;
- seven (7) of 14 or 50% of patients in the same dosing cohorts had an overall tumour response of Stable Disease and a reduction in the sum of target lesions and 57% of patients were progression free for greater than 16 weeks.

On March 8, 2016, the Company announced the following approved changes by the central ethics committee overseeing the Phase I/II study in Poland as it relates to the Phase II component of the study, which the Company intends to initiate:

- There will be no further escalations of L-DOS47 past cohort 16. If there are no further dose limiting toxicities, the cohort 16 dose, 13.55 µg/kg, will be the dose administered to patients in the Phase II dose.
- The safety profile supports a more frequent administration of L-DOS47. After reviewing safety, pharmacokinetic and immunogenicity data, L-DOS47 will be dosed twice weekly over 14 days (Days 1, 4, 8, 11) followed by a 7-day rest in the Phase II study.
- The number of patients in the Phase II study will be increased to 45 patients. Based on Simon's optimal two-stage design, 17 evaluable patients will be enrolled in the first stage of the Phase II component of the study. If there is/are ≥ 1 response(s) out of these initial 17 evaluable patients, 22 additional evaluable patients will need to be enrolled. To obtain 39 patients evaluable for response, enrolment of approximately 45 patients are needed.

On April 21, 2016, the Company announced the approval by the Trial Steering Committee to initiate the Phase II component of the LDOS002 study. On April 28, 2016, the Company announced the enrolment of the first patient in the Phase II component of the LDOS002 study. The first Phase II patient was dosed on May 10, 2016 and has now completed their first L-DOS47 cycle.

Although the Phase II L-DOS47 regimen has been well tolerated by patients enrolled in the first stage of the study, an improvement in potential benefit to patients compared to the Phase I regimen (L-DOS47 dosed once weekly over 14 days (Days 1, 8) followed by a 7-day rest) has not been observed. The potential complications associated with frequent intravenous administrations in LDOS002 does not support the potential benefit to patients, past cycle four. As a result, the LDOS002 protocol was amended to limit the number of dosing cycles to a maximum of 6 cycles. Patients are currently being followed for efficacy evaluation to determine if the second stage of the study will be open to enrolment. Following a review of the Phase II dataset, the Company will determine if they will pursue a clinical strategy of L-DOS47 as a monotherapy in NSCLC.

Following the review of clinical data collected to date, L-DOS47 continues to be well tolerated. The data also suggests that L-DOS47 may provide a clinical benefit for certain patients. Enrolment in the first stage of the Phase II component of study LDOS002 (n=21) has been completed. A Trial Steering Committee Meeting will be organized before the end of the year to review safety and efficacy data to determine next steps.

The Company continues to have insufficient cash resources to see the entire LDOS002 European Phase I/II clinical study in Poland through to completion. Given the Company's limited current cash resources and the possibility of not being able to obtain additional financing on a timely basis, the Company may be required to reduce, delay or cancel one or more of its planned research and development programs, including clinical trials along with further reductions in overhead, any of which could impair the current and future value of the business.

#### *Phase II clinical study ("LDOS003")*

A potential secondary yet unproven aspect of L-DOS47 action is the observation that an acidic pH microenvironment (< pH 6.8) may limit the effectiveness of weakly basic cytotoxic drugs employed in treatment of lung and other solid tumours. An acidic microenvironment is associated with protonation of these agents and decreased uptake and alkalisation can result in enhanced agent uptake and cytotoxicity. Furthermore, extracellular acidity may also inhibit the active transport of some drugs. This raises the possible application of L-DOS47 to combination cancer therapies with agents which have little or no overlapping toxicities.

This study is designed to determine the possible chemo-enhancing properties of L-DOS47. The possibility of combining L-DOS47 with a weakly basic agent like vinorelbine may improve therapeutic outcomes for cancer patients. The vinorelbine/cisplatin combination is used as a first-line treatment for lung adenocarcinoma.

The Company has initiated a Phase IIb, open-label, randomized study in male and female patients aged  $\geq 18$  years old with metastatic lung adenocarcinoma. The staging will be conducted according to Tumour Node Metastases (TNM), 8<sup>th</sup> Edition. In Part 1 of the study (Dose Escalation), patients will receive eight (8) doses of L-DOS47 over four (4) cycles. On Day 1 and Day 8 of each cycle, L-DOS47 (administered as an intravenous (“IV”) infusion) will be administered 24 hours before vinorelbine/cisplatin. Once the maximum tolerated dose of L-DOS47 as an adjunct to vinorelbine/cisplatin is determined, patients in Part 2 of the study (Randomized Treatment) will be randomly assigned to receive L-DOS47 in combination with vinorelbine/cisplatin or vinorelbine/cisplatin alone. Six (6) sites have been identified in Poland and the Ukraine. Competent Authority and Ethics Committee approvals are anticipated in the first quarter of 2018.

The Company has insufficient supply of L-DOS47 to complete the LDOS003 study. As a result, the Company plans to manufacture another batch of drug product in the next fiscal year to support the completion of the study and other planned studies. Completion of the study will depend on the successful release and availability of new drug product.

Given the Company’s limited current cash resources and the possibility of not being able to obtain additional financing on a timely basis, the Company may be required to reduce, delay or cancel one or more of its planned research and development programs, including clinical trials along with further reductions in overhead, any of which could impair the current and future value of the business.

### **Commercialization**

The Company’s DOS47 commercialization objective is to eventually enter into a strategic partnering alliance with a large pharmaceutical company, on an individual or multiple drug candidate basis, such as L-DOS47 or any potential new DOS47 drug product candidate. In the meantime, the Company will continue to gather as much value-adding clinical data/findings, which demonstrate the safety and efficacy of L-DOS47 in patients or any other new potential DOS47 drug candidate so as to maximize value for shareholders when entering into a strategic partnering alliance.

### **Market and Competition**

Based on information published in “Key Statistics for Lung Cancer” by the American Cancer Society ([www.cancer.org](http://www.cancer.org)), lung cancer accounts for about one out of four of all cancer deaths and is by far the leading cause of cancer death among men and women in the U.S. It is estimated that in 2017 there will be over 222,500 new lung cancer cases.

If detected early, surgical removal of the cancerous tissue is currently a patient’s best option. However, in the vast majority of cases, the cancer is not typically identified until it has advanced to a level at which surgical intervention is no longer an option. In the cases of inoperable, locally advanced, recurrent or metastatic NSCLC and with no known targetable mutations, treatment strategies consist of one or more of today’s leading chemotherapeutic drug regimens for lung cancer (e.g. platinum therapy together with certain leading chemotherapeutic drugs). Typically, these regimens relieve symptoms and, at best, delay progression of the disease.

Disease progression, even with targeted therapies, is highly likely to occur, and there are no clear guidelines and/or indications once such therapies fail. Maintenance therapy following the induction of first-line therapy is also a treatment strategy gaining support.

Immunotherapies such as immune checkpoint inhibitors that target Programmed Death 1 (“PD-1”) or its ligands, Programmed Death Ligand 1 or 2 (“PD-L1” and “PD-L2”, respectively) are showing significant clinical successes in NSCLC. On March 4, 2015 the FDA approved Nivolumab, the generic name for the trade drug named Opdivo®, which targets PD-1 for the treatment of metastatic squamous NSCLC with progression on or after platinum-based chemotherapy. On October 2, 2015, the FDA granted accelerated approval for Pembrolizumab, the generic name for the trade drug named Keytruda®, which targets PD-1 to treat patients with advanced metastatic NSCLC whose disease has progressed after other treatments and with tumours that express PD-L1. Anti-PD-L1 drugs such as MPDL3280A from Roche are also advancing rapidly through late stage clinical trials.

In 2015, three randomized Phase III trials found the immune checkpoint inhibitors nivolumab and pembrolizumab to have superior efficacy and less toxicity compared with second-line docetaxel chemotherapy in patients with NSCLC. For the first time, agents blocking a single pathway have shown significant benefit across multiple tumour types, with US Food and Drug Administration (FDA) approval in NSCLC, melanoma, and bladder and renal cell carcinoma. Now more than 1,000 immune checkpoint clinical trials are underway. Many possible treatment avenues are being explored with immune checkpoint inhibitors, including combinations with radiation, chemotherapy, targeted therapy, and other checkpoint inhibitors. Some studies are also investigating checkpoint inhibitors as front-line therapy.

As of March 2017, the FDA had approved five checkpoint inhibitor drugs: ipilimumab (Yervoy®), pembrolizumab (Keytruda®), nivolumab (Opdivo®), atezolizumab (Tecentriq®) and avelumab (Bavencio®).

On May 10, 2017, the FDA granted accelerated approval to pembrolizumab (KEYTRUDA®, Merck and Co., Inc.) in combination with pemetrexed and carboplatin for the treatment of patients with previously untreated metastatic non-squamous non-small cell lung cancer (NSCLC). Approval was based on a cohort (G1) of patients enrolled in an open-label, multicenter, multi-cohort study

(KEYNOTE-021). As a result of these developments in the treatment of NSCLC, the Company is currently reassessing its L-DOS47 clinical program given that: (a) its target therapeutic indication, being inoperable, locally-advanced, recurrent or metastatic NSCLC, may be a good candidate to combine with the emerging best-in-class immunotherapies; and (b) leading therapeutics for such oncology applications have commonly been high revenue generators for the pharmaceutical sector.

Technological competition from pharmaceutical companies, biotechnology companies and university researchers is intense and is expected to continue to be very intense. Many competitors and potential competitors have substantially greater product development capabilities and financial, scientific, marketing and human resources than the Company, providing them with a competitive advantage over the Company.

### ***The Biphasix™ Topical Formulation System***

The Biphasix™ Topical Formulation System is a platform technology which the Company acquired and further developed for microencapsulating therapeutic compounds in multilayered, lipid-based microvesicles. These microvesicles have complex structures that include a variety of compartments into which drug molecules can be integrated. The principal application of the technology is in the preparation of topical dosage forms for the dermal (into the skin) or mucosal (into the mucosal tissues) delivery of large molecular weight drug compounds.

#### *Topical Interferon Alpha-2b*

The Company received investigational new drug (“IND”) approval by the FDA to conduct a U.S. Phase II/III clinical trial of Topical Interferon Alpha-2b in low-grade cervical dysplasia patients, as well as Clinical Trial Application (“CTA”) approval by the Bundesinstitut für Arzneimittel und Medizinprodukte and conditional CTA approval by the Medicines and Healthcare Regulatory Authority to conduct an identical European Phase III confirmatory trial in Germany and/or the United Kingdom, respectively.

Due to a lack of funding, a decision was made by the Company in fiscal 2012 to downsize and eventually close the Saskatoon laboratory which supported the Topical Interferon Alpha-2b drug development program, and focus any ongoing activities to sourcing and qualifying alternative interferon alpha-2b raw material samples, and finding suitable strategic partner(s) who would be willing to license or acquire the product and support the remaining development costs through to commercial launch. In 2016, the Company ceased all activities related to Topical Interferon Alpha-2b, other than maintaining existing intellectual property associated with Topical Interferon Alpha-2b.

On December 23, 2016, the Company announced, it signed an exclusive out-license agreement with Xisle for the Company's late-stage, Biphasix™ technology platform, including the lead product candidate, interferon alpha. Xisle is responsible for the continued clinical development and subsequent commercialization of the product for the treatment of HPV-induced, low-grade, cervical intraepithelial lesions. As part of its asset development strategy, Xisle has initiated collaboration with senior pharmaceutical executives at Altum Pharmaceuticals Inc., who possess regulatory, clinical, and product development expertise. Under the terms of the agreement, Xisle paid an up-front fee of \$125,000 USD and agreed to pay subsequent milestone payments as they advance the technology to registration and market approvals and royalties. As part of the agreement, Helix retains marketing rights for Belarus, Bulgaria, Czech Republic, former Eastern Germany, Hungary, Moldova, Poland, Romania, Russia, Slovakia and Ukraine. In addition, the Company also retains non-exclusive rights for co-promotion in Canada.

The Company subsequently assigned the marketing rights which it retained to HIO, its wholly-owned subsidiary in Poland pursuant to an agreement between the Company and HIO with the agreement being subject to the restrictions and limitations associated with the out-license agreement signed between the Company and Xisle. In addition, HIO will be responsible for commercialization with milestone and royalty payments to be paid back to the Company upon successful product development through to commercialization.

## **SELECTED FINANCIAL INFORMATION AND SUMMARY OF QUARTERLY RESULTS**

Net loss and total comprehensive loss, over the last eight quarters, has ranged from a high of \$3,287,000 in fiscal Q1 2017 to a low of \$1,241,000 in fiscal Q4 of 2017 with fluctuations mainly dependant on the level of research and development activities and operating, general and administration expenses and the availability of cash reserves. The lower Q4 fiscal 2017 net loss and comprehensive loss reflects the Company's initiatives to cut costs and reduce expenditures in order to preserve cash.

The higher operating, general and administration expenditures in Q1 2017 reflects higher CEO related expenses, legal, investor and media relations and other consulting arrangements associated mainly with ongoing efforts by the Company to raise financing. The higher operating, general and administration expenditures in Q1 of fiscal 2016 were mainly the result of stock-based compensation expense for options granted to directors of the Company. The lower operating, general and administration expenses in Q1 2018 is the result of the Company's cost cutting measures.

The Company closed two private placements during the three-month period ended October 31, 2017 for gross proceeds of \$5,221,000. The Company closed several private placements during the last fiscal year (in Q4 2017 for gross proceeds of approximately \$3,029,000; in Q3 2017 for gross proceeds of \$1,930,000; in Q2 2017 for gross proceeds of \$1,824,000 and in Q1

2017 for gross proceeds of \$993,000). In Q4 2016, the Company closed a private placement for gross proceeds of \$1,825,000 and, in fiscal Q3 2016, the Company closed a private placement for gross proceeds of \$4,658,000.

(thousand \$, except per share information)								
	Q1	Q4	Q3	Q2	Q1	Q4	Q3	Q2
	2018	2017	2017	2017	2017	2016	2016	2016
Research and development expense	1,764	1,911	1,932	1,911	2,295	1,729	1,507	1,246
Operating, general and admin expense	526	873	944	873	1,008	872	748	957
Net loss and total comprehensive loss	-2,303	-2,618	-2,913	-2,618	-3,287	-2,604	-2,243	-2,226
Loss per share - basic & fully diluted	-0.02	-0.03	-0.03	-0.03	-0.04	-0.03	-0.02	-0.03
Cash	3,175	1,423	1,323	1,423	2,397	3,654	4,929	2,523
Working capital (deficiency)	1,674	-504	-1,994	-612	595	2,929	3,885	1,980

## RESULTS FROM OPERATIONS

### *Net loss and total comprehensive loss from continuing operations*

The Company recorded a net loss and total comprehensive loss of \$2,303,000 (\$0.02 loss per common share) and \$3,287,000 (\$0.04 loss per common share) for the three-month periods ended October 31, 2017 and 2016, respectively.

### *Research & development*

Research and development costs for the three-month periods ended October 31, 2017 and 2016 totalled \$1,764,000 and \$2,268,000, respectively.

The following table outlines research and development costs expensed for the Company's significant research and development projects for the three-month periods ended October 31:

	2017	2016
L-DOS47	\$ 1,482	\$ 1,765
V-DOS47	113	149
Corporate research and development expenses	98	280
Trademark and patent related expenses	99	71
Depreciation expense	55	30
Polish government grant subsidy (V-DOS47)	(83)	(27)
	\$ 1,764	\$ 2,268

L-DOS47 research and development expenses for the three-month periods ended October 31, 2017 and 2016 totalled \$1,482,000 and \$1,765,000, respectively. L-DOS47 research and development expenditures relate primarily to the Company's LDOS002 European Phase I/II clinical study in Poland and the LDOS001 U.S. Phase I clinical study in the U.S in addition to some preliminary expenditures related to the Company's LDOS003 Phase II clinical study in Poland and the Ukraine that the Company plans to commence enrolment in early 2018.

V-DOS47 research and development expenses for the three-month periods ended October 31, 2017 and 2016 totalled \$113,000 and \$149,000, respectively. The Company's wholly owned subsidiary in Poland has entered into a grant funding agreement with the PNCRD for research and development expenditures associated with V-DOS47. The Company's subsidiary received \$83,000 and \$27,000 in the three-month periods ended October 31, 2017 and 2016, respectively, from the PNCRD.

Corporate research and development expenses for the three-month periods ended October 31, 2017 and 2016 and totalled \$98,000 and \$280,000, respectively. The decrease in spending is the result of headcount reductions and external consulting contracts.

Trademark and patent related expenses for the three-month periods ended October 31, 2017 and 2016 totalled \$99,000 and \$71,000, respectively. The Company continues to ensure it adequately protects its intellectual property.

### *Operating, general and administration*

Operating, general and administration expenses for the three-month periods ended October 31, 2017 and 2016 totalled \$526,000 and \$1,008,000, respectively.

The decrease in operating, general and administration expenses reflects various ongoing cost cutting initiatives.

## **CRITICAL ACCOUNTING ESTIMATES**

The preparation of financial statements in conformity with IFRS requires management to make judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets and liabilities, revenue and expenses and the related disclosures of contingent assets and liabilities and the determination of the Company's ability to continue as a going concern. Actual results could differ materially from these estimates and assumptions. The Company reviews its estimates and underlying assumptions on an ongoing basis. Revisions are recognized in the period in which the estimates are revised and may impact future periods.

The areas involving a higher degree of judgment or complexity, or areas where assumptions and estimates are significant to the Company's financial statements have been set out in Note 1 of the Company's condensed unaudited interim consolidated financial statements for the three-month periods ended October 31, 2017 and 2016, respectively.

## **SIGNIFICANT ACCOUNTING POLICIES**

The significant accounting policies used in preparing the Company's consolidated financial statements are described in Note 2 of the Company's condensed unaudited interim consolidated financial statements for the three-month periods ended October 31, 2017 and 2016, except for those related accounting policies and methods of computation related to any new accounting standards and pronouncements.

## **NEW ACCOUNTING STANDARDS AND PRONOUNCEMENTS NOT YET ADOPTED**

New accounting standards and pronouncements issued but not yet effective up to the date of issuance of the Company's consolidated financial statements are listed below. This listing includes standards and interpretations issued, which the Company reasonably expects to be applicable at a future date. The Company intends to adopt those standards when they become effective. Certain pronouncements have been issued by the IASB or International Financial Reporting Interpretations Committee. Many of these updates are not applicable or are inconsequential to the Company and have been excluded from the discussion below:

### ***IFRS 9, Financial Instruments***

The IASB has issued a new standard, IFRS 9, Financial Instruments ("IFRS 9"), which will ultimately replace IAS 39, Financial Instruments: Recognition and Measurement ("IAS 39"). The project had three main phases: classification and measurement, impairment and general hedging. The standard becomes effective for annual periods beginning on or after January 1, 2018 and is to be applied retrospectively. Early adoption is permitted. The Company is evaluating the impact of the new standard on its results of operations, financial position and disclosures.

### ***IFRS 15, Revenue from Contracts with Customers***

The IASB has issued a new standard, IFRS 15, Revenue from Contracts with Customers ("IFRS 15"). IFRS 15 contains a single model that applies to contracts with customers and two approaches to recognizing revenue: at a point in time or over time. The model features a contract-based five-step analysis of transactions to determine whether, how much and when revenue is recognized. New estimates and judgmental thresholds have been introduced, which may affect the amount and/or timing of revenue recognized. The standard becomes effective for annual periods beginning on or after January 1, 2018. The Company is evaluating the impact of the new standard on its results of operations, financial position and disclosures.

### ***IFRS 16, Leases***

In January 2016, the IASB has issued IFRS 16 *Leases* ("IFRS 16"), its new leases standard that requires lessees to recognize assets and liabilities for most leases on their balance sheets. Lessees applying IFRS 16 will have a single accounting model for all leases, with certain exemptions. Lessor accounting is substantially unchanged. The new standard will be effective from January 1, 2019 with limited early application permitted. The Company is evaluating the impact of the new standard on its results of operations, financial position and disclosures.

## **LIQUIDITY AND CAPITAL RESOURCES**

Since inception, the Company has mainly relied on financing its operations from public and private sales of equity. The Company does not have any credit facilities and is therefore not subject to any externally imposed capital requirements or covenants. The Company manages its liquidity risk by continuously monitoring forecasts and actual cash flow from operations and anticipated investing and financing activities.

The Company reported a consolidated net loss and total comprehensive loss of \$2,303,000 for the three-month period ended October 31, 2017 (October 31, 2016 - \$3,287,000). As at October 31, 2017 the Company had working capital of \$1,674,000,

shareholders' equity of \$2,129,000 and a deficit of \$157,683,000. As at July 31, 2017 the Company had a working capital deficiency of \$504,000, shareholders' deficiency of \$17,000 and a deficit of \$155,380,000.

In order for the Company to advance its various planned preclinical and clinical research and development activities and pay for its overhead costs, the Company will need to raise approximately \$20,000,000 to \$25,000,000 over the next two fiscal years. Of this amount, planned capital expenditures are negligible totalling approximately \$31,000.

The Company established a cost cutting plan and worked with vendors to manage its cash position while ensuring vendors continued providing services while being paid, albeit over a longer period of time than previously agreed terms. The Company continues to work with its vendor base and more specifically, one vendor in particular, that oversees the Company's clinical study in Poland. The two private placements the Company closed during the three month-period ended October 31, 2017 for gross proceeds totalling \$5,221,000 improved the Company's working capital positions. Nevertheless, the Company's cash reserves of \$3,175,000 as at October 31, 2017 are insufficient to meet anticipated cash needs for working capital and capital expenditures through the next twelve months, nor are they sufficient to see the current or any planned research and development initiatives through to completion. Though the funds raised have assisted the Company in dealing with the working capital deficiency, additional funds are required to advance the various clinical and preclinical programs and pay for the Company's overhead costs. To the extent that the Company does not believe it has sufficient liquidity to meet its current obligations, management considers securing additional funds, primarily through the issuance of equity securities of the Company, to be critical for its development needs.

The Company's long-term liquidity depends on its ability to access the capital markets, which depends substantially on the success of its ongoing research and development programs, as well as economic conditions relating to the state of the capital markets generally. Accessing the capital markets can be particularly challenging for companies that operate in the biotechnology industry. The Company has predominately raised funds utilizing the services of ACM Alpha Consulting Management EST ("ACMest") and on September 8, 2017 entered into an agreement with ACMest and Oakbridge Capital Advisors Ltd., from London, England to assist in raising capital for the Company.

While the Company has been able to raise equity financing in recent years, there can be no assurance that additional funding by way of equity financing will continue to be available. Any additional equity financing, if secured, would result in dilution to the existing shareholders and such dilution may be significant. The Company may also seek additional funding from or through other sources, including technology licensing, co-development collaborations, mergers and acquisitions, joint ventures, and other strategic alliances, which, if obtained, may reduce the Company's interest in its projects or products or result in significant dilution to existing shareholders. The Company may also seek additional funding from government grants. There can be no assurance, however, that any alternative sources of funding will be available. The failure of the Company to obtain additional financing on a timely basis may result in the Company reducing, delaying or cancelling one or more of its planned research, development and/or marketing programs, including clinical trials, further reducing overhead, or monetizing non-core assets, any of which could impair the current and future value of the business or cause the Company to consider ceasing operations and undergoing liquidation.

Given the Company's conclusion about the insufficiency of its cash reserves, significant doubt may be cast about the Company's ability to continue operating as a going concern. The continuation of the Company as a going concern for the foreseeable future depends mainly on raising sufficient capital, and in the interim, reducing, where possible, operating expenses (including making changes to the Company's research and development plans), including the delay of one or more of the Company's research and development programs, further reducing overhead and the possible disposition of assets.

The Company had a total number of, 100,062,079 common shares issued and outstanding as at October 31, 2017 (July 31, 2017 – 90,059,279 common shares).

**RELATED PARTY TRANSACTIONS**

The key management personnel of the Company includes the Chief Executive Officer, Chief Financial Officer, Chief Scientific Officer and the Chief Operating Officer.

The following table summarizes key management personnel compensation for the three-month periods ended October 31:

	2017	2016
Compensation	\$ 209	\$ 434
Stock-based compensation	-	(15)
	\$ 209	\$ 419

The negative stock based compensation represents a reversal of expense from option cancellations.

The following table summarizes directors' compensation for the three-month periods ended October 31:

	2017	2016
Director's fees	\$ 80	\$ 81
Stock-based compensation	–	15
Consulting fees	–	142
	\$ 80	\$ 238

The Company entered into a consulting agreement with the Chairman of the Board to act as Chief Executive Officer of the Company. The agreement had a twelve-month term which expired on March 31, 2017.

The following table summarizes the board observer's compensation for the three-month periods ended October 31:

	2017	2016
Financial and investor relations agreement	\$ 128	\$ 134
Finder fee commissions	653	124
	\$ 781	\$ 258

The Company entered into a non-exclusive financial and investor relations agreement with ACM Alpha Consulting Management EST ("ACMest"), effective May 1, 2012. On March 7, 2014, Mr. Andreas Kandziora became an Observer to the Board of Directors of the Company. Mr. Kandziora was also appointed to the Supervisory Board of the Company's wholly-owned Polish subsidiary, Helix Immuno-Oncology. Mr. Kandziora is President and CEO of ACMest. During the 2017 fiscal year, the Board of Directors of the Company appointed Mrs. Veronika Kandziora, the spouse of Mr. Kandziora, as Corporate Secretary of the Company.

Related party transactions are at arm's length and recorded at the amount agreed to by the related parties.

## FINANCIAL INSTRUMENTS

### *Fair value hierarchy*

Financial instruments recorded at fair value on the balance sheet are classified using a fair value hierarchy that reflects the significance of the inputs used in making the measurements. The fair value hierarchy has the following levels:

- Level 1 reflects valuation based on quoted prices observed in active markets for identical assets or liabilities;
- Level 2 reflects valuation techniques based on inputs that are quoted prices of similar instruments in active markets; quoted prices for identical or similar instruments in markets that are not active; inputs other than quoted prices used in a valuation model that are observable for that instrument; and inputs that are derived principally from or corroborated by observable market data by correlation or other means; and
- Level 3 reflects valuation techniques with significant unobservable market inputs.

A financial instrument is classified to the lowest level of the hierarchy for which a significant input has been considered in measuring fair value. The financial instrument in the Company's financial statements, measured at fair value, is cash.

### *Fair value*

The fair value of financial instruments as at October 31, 2017 and July 31, 2017 approximates their carrying value because of the near-term maturity of these instruments.

## INTELLECTUAL PROPERTY

Patents and other proprietary rights are very valuable to the Company, even though the patent positions of biotechnology companies may be uncertain and involve complex legal and factual issues. The Company has no assurance that any of its patent applications will result in the issuance of any patents. Even issued patents may not provide the Company with a competitive advantage against competitors with similar technologies, or who have designed around the Company's patents. Furthermore, the Company's patents may be struck down if challenged. Intellectual property laws do not protect intellectual property to the same extent from one country to another.

Because of the substantial length of time and expense associated with developing new products, the pharmaceutical, medical device, and biotechnology industries place considerable importance on obtaining patent protection for new technologies, products, and processes. The Company's policy is to file patent applications to protect inventions, technology, and improvements that are important to the development of our business and with respect to the application of our products and technologies to the treatment of a number of disease indications. The Company's policy also includes regular reviews related to the development of each technology and product in light of its intellectual property protection, with the goal of protecting all key research and developments by patent.



The Company seeks intellectual property protection in various jurisdictions around the world and owns patents and patent applications relating to products and technologies in the United States, Canada, Europe and other jurisdictions. The scope and duration of our intellectual property rights vary from country to country depending on the nature and extent of our intellectual property filings, the applicable statutory provisions governing the intellectual property, and the nature and extent of our legal rights. The Company will continue to seek intellectual property protection as appropriate and require our employees, consultants, outside scientific collaborators, and sponsored researchers to enter into confidentiality agreements with us that contain assignment of invention clauses outlining ownership of any intellectual property developed during the course of the individual's relationship with us.

### ***Tumor Defense Breaker™***

On September 29, 2016 the Company filed a Canadian Trade Mark Application for "TUMOR DEFENSE BREAKER". It is planned to expand this trademark in all major markets and territories where will aim to market the products once they receive marketing approval by appropriate regulatory authorities. On May 1, 2017, the Company was notified that the trade mark application had been approved. A similar application was made in Europe which was not accepted and the Company is assessing whether it will appeal this decision.

### ***DOS47, L-DOS47 and V-DOS47***

The Company currently owns two U.S. patents in respect of the DOS47 technology, and also has also licensed patent rights from the NRC for the antibody component of L-DOS47. With respect to non-U.S. patents, the Company owns 52 DOS47 related patents in other jurisdictions with a number of patent applications in countries around the world. The Company has recently filed a joint patent application in the U.S. with Amorfix to cover the antibody-DOS47 conjugates derived from their collaboration. A new U.S. patent application to cover new features of the DOS47 technology was filed by the Company during fiscal 2013. During January 2015, an additional U.S. patent application covering specific L-DOS47 manufacturing and novel features was filed. During fiscal 2017, a new U.S. patent application protecting the novel use of L-DOS47 in restoring T cell function for therapeutic application was filed. In addition, two US patents covering anti-VEGFR2 antibodies and their use in DOS47 conjugates (V-DOS4) were filed.

### ***Cell Based Therapy***

The company has recently filed a joint patent application with NRC to protect the use of an antibody for use in cell based therapies. In addition, the company has also filed new patent application covering the use of anti-VEGFR2 antibodies in cell based therapy in July 2017. The Company is currently in discussion with third parties to license additional intellectual properties to strengthen the company's portfolio.

### ***Biphaxis™***

The Company, until recently, owned six U.S. Biphaxis™ patents.

On December 23, 2016, the Company announced, it signed an exclusive out-license agreement with Xisle for the Company's late-stage, Biphaxis™ technology platform, including the lead product candidate, interferon alpha. Xisle is responsible for the continued clinical development and subsequent commercialization of the product for the treatment of HPV-induced, low-grade, cervical intraepithelial lesions. As part of its asset development strategy, Xisle has initiated collaboration with senior pharmaceutical executives at Altum Pharmaceuticals Inc., who possess regulatory, clinical, and product development expertise. Under the terms of the agreement, Xisle paid an up-front fee of \$125,000 USD and agreed to pay subsequent milestone payments as they advance the technology to registration and market approvals and royalties. As part of the agreement, Helix retains marketing rights for Belarus, Bulgaria, Czech Republic, former Eastern Germany, Hungary, Moldova, Poland, Romania, Russia, Slovakia and Ukraine. In addition, the Company also retains non-exclusive rights for co-promotion in Canada.

The Company subsequently assigned the foregoing marketing rights which it retained to HIO, its wholly -owned subsidiary in Poland pursuant to an agreement between the Company and HIO with the agreement being subject to the restrictions and limitations associated with the out-license agreement signed between the Company and Xisle. In addition, HIO will be responsible for commercialization with milestone and royalty payments to be paid back to the Company upon successful product development through to commercialization.

## **OFF-BALANCE SHEET ARRANGEMENTS**

The Company has no material off-balance sheet arrangements.

## QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The Company's main objectives when managing capital are to ensure sufficient liquidity to finance research and development activities, clinical trials, ongoing administrative costs, working capital and capital expenditures. The Company includes cash and components of shareholders' equity, in the definition of capital. The Company endeavours not to unnecessarily dilute shareholders when managing the liquidity of its capital structure.

### **Currency risk**

The Company operates internationally and is exposed to foreign exchange risks from various currencies, primarily the Euro and U.S. dollar. Foreign exchange risks arise from the foreign currency translation of the Company's integrated foreign operation in Poland. In addition, foreign exchange risks arise from purchase transactions, as well as recognized financial assets and liabilities denominated in foreign currencies.

Balances in foreign currencies are as follows as at:

	October 31, 2017			July 31, 2017		
	EUR	USD	PLN	EUR	USD	PLN
Cash	8,000	–	447,000	32,000	1,000	276,000
Accounts receivable	–	–	115,000	–	–	178,000
Accounts payable	(465,000)	(137,000)	(318,000)	(468,000)	(229,000)	(201,000)
Accruals	(192,000)	–	(18,000)	(217,000)	(24,000)	(99,000)
Net foreign currencies	(649,000)	(137,000)	226,000	(653,000)	(252,000)	(154,000)
Closing exchange rate	1.5014	1.2893	0.3531	1.4719	1.2485	0.3415
Impact of 1% change in exchange rate +/-	10,000	2,000	+/-1,000	9,000	3,000	+/- 1,000

Any fluctuation in the exchange rates of the foreign currencies listed above could have an impact on the Company's results from operations; however, they would not impair or enhance the ability of the Company to pay its foreign-denominated expenses.

### **Credit risk**

Credit risk is the risk of a financial loss to the Company if a customer or counterparty to a financial instrument fails to meet its contractual obligation.

The table below breaks down the various categories that make up the Company's accounts receivable balances:

	October 31, 2017	July 31, 2017
Government related – HST/VAT	\$ 58,000	\$ 177,000
Research and development investment tax credits	318,000	430,000
Other	33,000	23,000
	\$ 409,000	\$ 630,000

### **Interest rate risk**

Interest rate risk is the risk that future cash flows of a financial instrument will fluctuate because of changes in interest rates, which are affected by market conditions. The Company is exposed to interest rate risk arising from fluctuations in interest rates received on its cash. The Company does not have any credit facilities and is therefore not subject to any debt related interest rate risk.

The Company manages its interest rate risk by maximizing the interest income earned on excess funds while maintaining the liquidity necessary to conduct its operations on a day-to-day basis. Any investment of excess funds is limited to risk-free financial instruments. Fluctuations in the market rates of interest do not have a significant impact on the Company's results of operations due to the relatively short-term maturity of any investments held by the Company at any given point in time and the low global interest rate environment. The Company does not use derivative instruments to reduce its exposure to interest rate risk.

### **Liquidity risk**

Liquidity risk is the risk that the Company will not be able to meet its obligations as they come due.

Since inception, the Company has mainly relied on financing its operations from public and private sales of equity. The Company does not have any credit facilities and is therefore not subject to any externally imposed capital requirements or covenants.

The Company manages its liquidity risk by continuously monitoring forecasts and actual cash flow from operations and anticipated investing and financing activities.

The Company's cash reserves of \$3,175,000 as at October 31, 2017 are insufficient to meet anticipated cash needs for working capital and capital expenditures through the next twelve months, nor are they sufficient to see the current research and development initiatives through to completion. To the extent that the Company does not believe it has sufficient liquidity to meet its current obligations, management considers securing additional funds primarily through equity arrangements to be of utmost importance.

The Company's long-term liquidity depends on its ability to access the capital markets, which depends substantially on the success of the Company's ongoing research and development programs, as well as economic conditions relating to the state of the capital markets generally. Accessing the capital markets is particularly challenging for companies that operate in the biotechnology industry.

## **OUTSTANDING SHARE DATA**

As at October 31, 2017, the Company had outstanding 100,062,079 common shares; warrants to purchase up to 32,331,475 common shares; and incentive stock options to purchase up to 930,000 common shares. As at July 31, 2017, the Company had outstanding 95,711,579 common shares; warrants to purchase up to 27,980,975 common shares; and incentive stock options to purchase up to 930,000 common shares.

## **DISCLOSURE CONTROLS AND PROCEDURES AND INTERNAL CONTROL OVER FINANCIAL REPORTING**

Management has designed the Company's disclosure controls and procedures to provide reasonable assurance that all relevant information is gathered, recorded, processed, summarized and reported to the Chief Executive Officer ("CEO") and the Chief Financial Officer ("CFO") of the Company so that appropriate decisions can be made within the time periods specified in securities legislation regarding public disclosure by the Company in its annual filings, interim filings or other documents or reports required to be filed or submitted by it under securities legislation.

Management has also designed internal controls over financial reporting ("ICFR") to provide reasonable assurance regarding the reliability of the Company's financial reporting and the preparation of financial statements for external purposes in accordance with IFRS. Because of its inherent limitations, ICFR can provide only reasonable assurance and may not prevent or detect misstatements. Further, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

### ***Material weakness previously disclosed but not yet remediated***

The termination of the Company's controller in the third fiscal quarter, whose position has not been filled, resulted in a lack of resources and has in turn impacted segregation of duties associated with the financial close and reporting process.

As at October 31, 2017, management has evaluated the effectiveness of the Company's disclosure controls and procedures and ICFR and have concluded they are not effective due to the above noted area of concern.

Management has concluded and the board has agreed, that when taking into account the Company's size and financial resources, the Company does not have sufficient scale of resources to warrant the hiring of additional staff to address this concern at this time and, accordingly, that there is a material weakness in the design of the Company's ICFR that has the potential to result in material misstatements in the Company's financial statements and that this should also be considered a weakness in the design and operating effectiveness of the Company's disclosure controls and procedures. This material weakness is considered to be a common area of deficiency for many smaller listed companies in Canada.

Although the CEO and CFO are not aware of the above deficiency having actually resulted in a material misstatement of a financial statement amount or disclosure, they have determined that, the deficiency could result in business and accounting practices that could put both the Company's reputation and its financial reporting at risk and lead to uncertainty whether control procedures are being carried out such that the Company's ICFR may fail to prevent or detect a material misstatement of a financial statement amount or disclosure on a timely basis or fail to disclose material information required to be disclosed under securities legislation within the time periods specified in securities legislation. However, there are several mitigating procedures and other factors which reduce the risk of a material misstatement in the financial statements, including substantive review of the financial statements by the Company's audit committee and day-to-day management involvement in operations and reporting.

## **RISKS AND UNCERTAINTIES**

Helix is subject to risks, events and uncertainties, or "risk factors", associated with being both a publicly traded company operating in the biopharmaceutical industry, and as an enterprise with several projects in the research and development stage. As a result of these risk factors, reported information and forward-looking information may not necessarily be indicative of future operating results or of future financial position, and actual results may vary from the forward-looking information or reported information. The Company cannot predict all of the risk factors, nor can it assess the impact, if any, of such risk factors on the Company's

business or the extent to which any factor, or combination of factors, may cause future results or financial position to differ materially from either those reported or those projected in any forward-looking information. Accordingly, reported financial information and forward-looking information should not be relied upon as a prediction of future actual results. Some of the risks and uncertainties affecting the Company, its business, operations and results which could cause actual results to differ materially from those reported or from forward-looking information include, either wholly or in part, those described elsewhere in this MD&A, as well as the following:

***The Company does not have any source of operating income and is dependent solely on outside sources of financing***

The Company's operations consist of research and development activities, which do not generate any revenue. Accordingly, the Company has no source of revenue, positive operating cash flow or operating earnings to subsidize its ongoing research and development and other operating activities and the ability of the Company to continue as a going concern is dependent upon the Company's ability to rely on cash on hand, and on outside sources of financing to fund its ongoing research and development and other operating activities. Such sources of financing involve risks, including that the Company will not be able to raise such financing on terms satisfactory to the Company or at all, and that any additional equity financing, if secured, would result in dilution to existing shareholders, and that such dilution may be significant. While the Company has been able to raise equity financing in recent years, there can be no assurance that additional funding by way of equity financing will continue to be available. Any additional equity financing, if secured, would result in dilution to the existing shareholders and such dilution may be significant. The Company may also seek additional funding from or through other sources, including technology licensing, co-development collaborations, mergers and acquisitions, joint ventures, and other strategic alliances, which, if obtained, may reduce the Company's interest in its projects or products or result in significant dilution to existing shareholders. The Company may also seek additional funding from government grants. There can be no assurance, however, that any alternative sources of funding will be available. The failure of the Company to obtain additional financing on a timely basis may result in the Company reducing, delaying or cancelling one or more of its planned research, development and/or marketing programs, including clinical trials, further reducing overhead, or monetizing non-core assets, any of which could impair the current and future value of the business or cause the Company to consider ceasing operations and undergoing liquidation. Given the Company's conclusion about the insufficiency of its cash reserves, significant doubt may be cast about the Company's ability to continue operating as a going concern. The continuation of the Company as a going concern for the foreseeable future depends mainly on raising sufficient capital, and in the interim, reducing, where possible, operating expenses (including making changes to the Company's research and development plans), including the delay of one or more of the Company's research and development programs, further reducing overhead and the possible disposition of assets.

***The Company has a history of losses and expects to continue to incur additional losses for the foreseeable future***

The Company's primary focus continues to be on its research and development of pharmaceutical product candidates. The research and development of pharmaceutical products requires the expenditure of significant amounts of cash over a relatively long-time period. The Company expects to continue to incur losses from continuing operations, for the foreseeable future. The Company's cumulative deficit as at October 31, 2017 is \$157,683,000. There can be no assurance that the Company will record earnings in the future.

***The Company requires additional funding***

The Company's cash reserves will not be sufficient for the Company to fully fund its existing European Phase I/II clinical trial with L-DOS47 in Poland or its U.S. Phase I trial or any of the Company's other ongoing research and development, operating activities, working capital or capital expenditures for the next twelve months.

The Company has no sources of external liquidity, such as a bank loan or line of credit. The Company will therefore continue to rely on equity financing to fund its ongoing research and development activities and other expenses for the foreseeable future.

Equity financing has historically been the Company's primary source of funding; however, the market for equity financings for companies such as the Company is challenging. While the Company has been able to raise equity financing in recent years, there can be no assurance that additional funding by way of equity financing will continue to be available. Any additional equity financing, if secured, would result in dilution to the existing shareholders which may be significant. The Company may also seek additional funding from or through other sources, including grants, technology licensing, co-development collaborations, disposition of assets, mergers and acquisitions, joint ventures, and other strategic alliances, which, if obtained, may reduce the Company's interest in its projects or products or result in significant dilution to existing shareholders. There can be no assurance, however, that any alternative sources of funding will be available.

The failure of the Company to obtain additional financing on a timely basis may result in the Company reducing, delaying or cancelling one or more of its planned research and development, including any clinical trials, further reducing overhead, or monetizing non-core assets, any of which could impair the current and future value of the business or cause the Company to consider ceasing operations and undergoing liquidation.

***The Company faces risks in connection with competition and technological change;***

The biotechnology and pharmaceutical industries are subject to rapid and substantial technological change. Technological competition from pharmaceutical companies, biotechnology companies and university researchers is intense and is expected to continue to be intense.

The rapid advancement of immunotherapies now has the potential to significantly change the treatment of cancer and may result in a reduction, which may be significant, in the potential patient population and/or treatment protocols available to chemotherapies and other treatments currently in development, such as the Company's primary drug product candidate, L-DOS47. Furthermore, developments in immunotherapies may require the Company to reposition its L-DOS47 drug product candidate from a front-line monotherapy to a combination therapy with immunotherapies or other treatment protocols, and any such repositioning, would likely result in additional expenses being incurred by the Company and in delays in the anticipated development timeline for L-DOS47, or in the Company determining that its L-DOS47 drug product candidate is no longer viable.

The Company cell based therapies initiative may face significant hurdles. The Company's effort is mainly at research proof-of-concept stage. It is possible that the selected targets or choice of antibodies are not optimal. This can delay the initiation of formal preclinical and clinical development significantly. The Company has chosen to develop cell based therapy for solid tumour. While there are many successful examples of cell based therapy treatment in hematological malignancies, similar success in solid tumour is less certain.

Many of the Company's competitors have substantially greater financial, technical and human resources and significantly greater experience in conducting preclinical testing and human clinical trials of product candidates, scaling up manufacturing operations and obtaining regulatory approvals of products. Accordingly, the Company's varying competitors may succeed in obtaining regulatory approval for products more rapidly. The Company's ability to compete successfully will largely depend on:

- the efficacy and safety profile of our product candidates relative to marketed products and other product candidates in development;
- our ability to develop and maintain a competitive position in the product categories and technologies on which we focus;
- the time it takes for our product candidates to complete clinical development and receive marketing approval;
- our ability to obtain required regulatory approvals;
- our ability to commercialize any of our product candidates that receive regulatory approval;
- our ability to establish, maintain and protect intellectual property rights related to our product candidates; and
- acceptance of any of our product candidates that receive regulatory approval by physicians and other healthcare providers and payers.

Competitors have developed and may develop technologies that could be the basis for products that challenge the differentiated nature and potential for best-in-class product development programs and discovery research capabilities of the DOS47 platform technology. Some of those products may have an entirely different approach or means of accomplishing the desired therapeutic effect than our product candidates and may be more effective or less costly than our product candidates. The success of our competitors and their products and technologies relative to our technological capabilities and competitiveness could have a material adverse effect on the future preclinical studies and clinical trials of our product candidates, including our ability to obtain the necessary regulatory approvals for the conduct of such clinical trials. This may further negatively impact our ability to generate future product development programs with improved pharmacological properties.

If we are not able to compete effectively against our current and future competitors, our business will not grow and our financial condition and operations will substantially suffer.

***The Company is conducting early stage research and development initiatives for products under development which may not be accepted by the market and may never generate revenue and the Company has limited sales, marketing and distribution experience***

The Company is conducting early stage research and development initiatives and is currently in the process of developing new products that require further time consuming and costly research and development. It will be a number of years, if ever, before its products in development begin to generate revenues, if at all. There can be no assurance that any of the drug product candidates will ever be successfully developed or commercialized.

Even with regulatory approval, the Company may not achieve market acceptance, which depends on a number of factors, including the establishment and demonstration in the medical community of the clinical utility of the Company's products, and their potential advantage over alternative treatment methods. There is also the risk that the actual market size or opportunity for the Company's drug candidates is not certain. Failure to gain market acceptance of either of the

Company's products currently under development or an incorrect estimate in the nature and size of their respective markets could have a material adverse effect on the Company.

The Company has limited sales, marketing and distribution experience, and there is no assurance that the Company will be able to establish adequate sales, marketing, and distribution capabilities or make arrangements with any collaborators, strategic partners, licensees, or others to perform such activities, or that such efforts will be successful. The Company's objective for its drug candidate products is to enter into strategic alliances with appropriate pharmaceutical partners. There can be no assurance that any such strategic alliance will be maintained or achieved, or if achieved, that it will result in revenue to the Company.

***The timing of the Company's internal goals and projected timelines may not be met***

The Company sets internal goals for and makes public statements regarding its expected timing of meeting the objectives material to its success, including the commencement, duration and completion of clinical trials and anticipated regulatory approvals. The actual timing of these forward-looking events can vary dramatically due to a number of factors, including, without limitation, delays in scaling-up of drug product candidates, delays or failures in clinical trials, additional data requirements from the regulators, the Company failing to obtain required financing, and other risks referred to herein. Without limiting the generality of the foregoing, it is possible that required regulatory approvals may be delayed or denied, including those related to undertaking or continuing clinical trials, manufacturing of drug products, and marketing such products.

The Company has expressed certain estimated timelines for its European Phase I/III clinical trials for L-DOS47 in Poland, the U.S. Phase I study. The timeline for the European Phase I/III trials and any future timelines are contingent on the Company having adequate financing to complete the trials and the assumption that the trials will be completed according to the current schedules. A failure to obtain necessary financing or a change in the schedule of the trials (which may occur if certain cost-deferral measures are taken, or due to factors beyond the Company's reasonable control, such as scheduling conflicts, the occurrence of serious adverse events, interruption of supplies of study drugs, withdrawals of regulatory approvals, or slow patient recruitment) could delay their commencement or completion, or result in their suspension or early termination, which could have a material adverse effect on the Company.

***The Company faces intellectual property risks, including the loss of patent protection, the potential termination of licences, the inability to protect proprietary property, and possible claims of infringement against the Company or against a third-party from whom the Company licenses intellectual property***

The Company's success depends, in part, on its ability to secure and protect its intellectual property rights and to operate without infringing on the proprietary rights of others or having third parties circumvent the rights owned or licensed by the Company. However, the Company cannot predict the enforceability of its patents or its ability to maintain trade secrets that may not be protected by patents. Patent risks include the fact that patent applications may not result in issued patents, issued patents may be circumvented, challenged, invalidated or insufficiently broad to protect the Company's products and technologies; blocking patents by third parties could prevent the Company from using its patented technology; it may be difficult to enforce patent rights, particularly in countries that do not have adequate legal enforcement mechanisms, and enforcing such rights may divert management attention and may cause the Company to incur significant expenses; and any expiry of an issued patent may negatively impact the underlying technology.

To protect its trade secrets, the Company enters into confidentiality undertakings with parties that have access to them, such as the Company's current and prospective distributors, collaborators, employees and consultants, but a party may breach the undertakings and disclose the Company's confidential information or competitors might learn of the information in some other way, which could have a material adverse effect on the Company.

The Company uses processes, technology, products, or information, the rights to certain of which are owned by others, such as a license from the NRC of the lung antibody used by the Company for L-DOS47. Termination or expiry of any licenses or rights during critical periods, and an inability to obtain them on commercially favourable terms or at all could have a material adverse effect on the Company and its drug candidates' development.

The Company operates in an industry that experiences substantial litigation involving the manufacture, use and sale of new products that are the subject of conflicting proprietary rights. The Company or one or more of its licensors may be subject to a claim of infringement of proprietary rights by a third party. It is possible that the Company's products and technologies do infringe the rights of third parties, and the Company or such licensor could incur significant expenses, and diversion of management attention, in defending allegations of infringement of proprietary rights, even if there is no infringement. Furthermore, the Company or such licensors may be required to modify its products or obtain licenses for intellectual property rights as a result of any alleged proprietary infringement. The inability to modify products or obtain licenses on commercially reasonable terms, in a timely manner or at all, could adversely affect the Company's business.

***The Company faces research and development risks, including the need to prove the Company's drug candidates are safe and effective in clinical trials***

The Company's drug candidates are complex compounds and the Company faces difficult challenges in connection with the manufacture of clinical batches of each of them, which could further delay or otherwise negatively affect the Company's planned clinical trials, or required regulatory approvals.

There is also the risk that the Company could obtain negative findings or factors that may become apparent during the course of research or development. The results from preclinical and clinical trials may not be predictive of results obtained in any ongoing or future clinical trials. A number of companies in the biotechnology and pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after achieving promising results in earlier trials and pre-clinical trials.

The timing and success of the Company's clinical trials also depend on a number of other factors, including, but not limited to: (a) obtaining additional financing, which is not assured; (b) sufficient patient enrolment, which may be affected by the incidence of the disease studied, the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the eligibility criteria for a patient to participate in the study and the rate of patient drop-out; (c) regulatory agency policies regarding requirements for approval of a drug, including granting permission to undertake proposed human testing; (d) the Company's capacity to produce sufficient quantities and qualities of clinical trial materials to meet the trial schedule; (e) performance by third parties, on whom the Company relies to carry out its clinical trials; and (f) the approval of protocols and/or protocol amendments.

Clinical trials are complex, expensive and uncertain, and have a high risk of failure, which can occur at any stage. Data obtained from pre-clinical and clinical trials may be interpreted in different ways, or be incorrectly reported, which could delay or prevent further development of the drug candidate studied. Failure to complete clinical trials successfully and to obtain successful results on a timely basis could have a material adverse effect on the Company.

Even if the Company's drug candidates successfully complete the clinical trials and receive the regulatory approval necessary to market the drug candidates to the public, there is also the risk of unknown side effects, which may not appear until the drug candidates are on the market and may result in delay or denial of regulatory approval or withdrawal of previous approvals, product recalls or other adverse events, which could materially adversely affect the Company.

While the Company continues to explore opportunities to expand its drug product pipeline with new DOS47-based therapeutics pending the identification of further tumour targeting agents, there can be no assurance that any such tumour targeting agents will be identified or that any new DOS47-based therapeutics will be developed.

***Difficulty in enrolling patients in the Company's clinical trials, could result in delays or cancellation of clinical trials***

As the Company's product candidates advance from preclinical testing to clinical testing, and then through progressively larger and more complex clinical trials, the Company will need to enroll an increasing number of patients that meet various eligibility criteria. There is significant competition for recruiting cancer patients in clinical trials, and the Company may not be able to enroll the patients it needs to complete clinical trials on a timely basis or at all. The factors that affect the Company's ability to enroll patients is largely uncontrollable and include, but are not limited to, the following:

- size and nature of the patient population;
- eligibility and exclusion criteria for the trial;
- design of the study protocol;
- competition with other companies for clinical sites or patients;
- the perceived risks and benefits of the product candidate under study;
- the patient referral practices of physicians; and
- the number, availability, location and accessibility of clinical trial sites.

***The Company is dependent on a number of third parties and the failure or delay in the performance of one of these third parties' obligations may adversely affect the Company***

The Company is dependent on third parties to varying degrees in virtually all aspects of its business, including without limitation, on contract research organizations, contract manufacturing organizations, clinical trial consultants, raw material suppliers, collaborative research consultants, regulatory affairs advisers, medical and scientific advisors, clinical trial investigators, business service providers and other third parties. Critical supplies may not be available from third parties on acceptable terms, or at all, including GMP grade materials. Service providers may not perform, or continue to perform, as needed, or be available to provide the required services on acceptable terms or at all. Any lack of or interruption in supplies of raw materials or services, or any change in supply or service providers or any inability to secure new supply or service providers, would have an adverse impact on the development and commercialization of the Company's products. For example, the Company has previously experienced delays in the manufacturing of both engineering and clinical batches of L-DOS47, which have in turn caused delays in the progression of its development program, and there

may be further delays. The Company relies on a third party for its supply of urease and if the contract with the third-party urease supplier is terminated early, the Company will have to find a new supplier of urease, as well as a new manufacturer of bulk drug product for future clinical testing programs. There can be no assurance that a new supplier or manufacturer can be contracted in a timely manner or at all, and this could negatively impact the Company's development plans for L-DOS47.

With respect to L-DOS47, the Company is currently dependent on, in addition to third party suppliers, manufacturers and consultants, the NRC and its license to the Company of a lung cancer antibody in order to develop and commercialize L-DOS47. Early termination of the license with NRC would have a material adverse effect on the further development of L-DOS47 and may require the cessation of such development, which would have a material adverse effect on the Company.

Given the Company's lack of financing, expertise, infrastructure and other resources to support a new drug product from clinical development to marketing, the Company also requires strategic partner support to develop and commercialize its drug candidates. There can be no assurance that such strategic partner support will be obtained upon acceptable terms or at all.

The Company relies heavily on contract manufacturers for the production of product required for its clinical trials, product formulation work, scaling-up experiments and commercial production. The Company may not be able to obtain new, or keep its current, contract manufacturers to provide these services. Even if the Company does, contract manufacturers may not be reliable in meeting its requirements for cost, quality, quantity or schedule, or the requirements of any regulatory agencies. The Company may not be able to manufacture products in quantities or qualities that would enable the Company to meet its business objectives, and failure to do so would materially adversely affect the Company's business.

If the Company can successfully develop markets for its products, the Company would have to arrange for their scaled-up manufacture. There can be no assurance that the Company will, on a timely basis, be able to make the transition from manufacturing clinical trial quantities to commercial production quantities successfully or be able to arrange for scaled-up commercial contract manufacturing. Any potential difficulties experienced by the Company in manufacturing scale-up, including recalls or safety alerts, could have a material adverse effect on the Company's business, financial condition, and results of operations.

***The marketability of the Company's products may be affected by delays and the inability to obtain necessary approvals, and following any market approval, the Company's products will be subject to ongoing regulatory review and requirements which may continue to affect their marketability, including but not limited to regulatory review of drug pricing, healthcare reforms or the payment and reimbursement policies for drugs by the various insurers and other payors in the industry***

The research, development, manufacture and marketing of pharmaceutical products are subject to regulation by the FDA, and comparable regulatory authorities in other countries. These agencies and others regulate the testing, manufacture, safety and promotion of the Company's products. The Company must receive applicable regulatory approval of a product candidate before it can be commercialized in any particular jurisdiction. Approval by a regulatory authority of one country does not ensure the approval by regulatory authorities of other countries. Changes in regulatory approval policies or regulations during the development period may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application, or may decide that our data are insufficient for approval, or require additional preclinical, clinical or other trials and place the Company's IND submissions on hold for an indeterminate amount of time. The development and regulatory approval process in each jurisdiction takes many years, requires the expenditure of substantial resources, is uncertain and subject to delays, and can adversely affect the successful development and commercialization of our drug candidates.

Even if the Company obtains marketing approval in a particular jurisdiction, there may be limits on the approval and the Company's products likely will be subject to ongoing regulatory review and regulatory requirements in that jurisdiction. Pharmaceutical companies are subject to various government regulations, including without limitation, requirements regarding occupational safety, laboratory practices, environmental protection and hazardous substance control, and may be subject to other present and future regulations.

The availability of reimbursement by governmental and other third-party payors, such as private insurance plans, will affect the market for any pharmaceutical product, and such payors tend to continually attempt to contain or reduce the costs of healthcare. Significant uncertainty exists with respect to the reimbursement status of newly approved healthcare products.



***The Company operates in an industry that is more susceptible than others to legal proceedings and, in particular, liability claims***

The Company operates in an industry that is more susceptible to legal proceedings than firms in other industries, due to the uncertainty involved in the development of pharmaceuticals. Defense and prosecution of legal claims can be expensive and time consuming, and may adversely affect the Company regardless of the outcome due to the diversion of financial, management and other resources away from the Company's primary operations. Negative judgments against the Company, even if the Company is planning to appeal such a decision, or even a settlement in a case, could negatively affect the cash reserves of the Company, and could have a material negative effect on the development of its drug products.

The Company may be exposed, in particular, to liability claims which are uninsured or not sufficiently insured, and any claims may adversely affect the Company's ability to obtain insurance in the future or result in negative publicity regarding the efficacy of its drug products. Such liability insurance is expensive, its ability is limited and it may not be available on terms that are acceptable to the Company, if at all.

The use of any of the Company's unapproved products under development, the use of its products in clinical trials, and, if regulatory approval is received, the sale of such products, may expose the Company to liability claims which could materially adversely affect the Company's business. The Company may not be able to maintain or obtain commercially reasonable liability insurance for future products, and any claims under any insurance policies may adversely affect its ability to maintain existing policies or to obtain new insurance on existing or future products. Even with adequate insurance coverage, publicity associated with any such claim could adversely affect public opinion regarding the safety or efficacy of the Company's products. As a result, any product liability claim or recall, including in connection with products previously sold by the Company through its former distribution business, could materially adversely affect the Company's business.

***If the Company were unable to maintain product liability insurance required by our third parties, the corresponding agreements would be subject to termination, which could have a material adverse impact on our operations.***

Some of our licensing and other agreements with third parties require or might require us to maintain product liability insurance. If the Company cannot maintain acceptable amounts of coverage on commercially reasonable terms in accordance with the terms set forth in these agreements, the corresponding agreements would be subject to termination, which could have a material adverse impact on the Company's operations.

***The Company is dependent upon key personnel; Director residency requirements***

The Company's ability to continue its development of potential products depends on its ability to attract and maintain qualified key individuals to serve in management and on the Board. However, the Company does not currently have a formal succession plan for members of its senior management team or for its Board and, because competition for qualified key individuals with experience relevant to the industry in which the Company operates is intense, the Company may not be able to attract and/or retain such personnel. Additionally, applicable corporate law requires that at least 25% of the Company's directors be resident Canadians, and the Company's articles provide that the Company cannot have fewer than five directors at any time.

Consequently, if the Company is unable to attract and/or loses and is unable to replace key personnel, its business could be negatively affected and, in particular, if the Company loses one or more of its three current resident Canadian directors in the future and is unable to find a sufficient number of resident Canadian directors to fill the resulting vacancy(ies), the Board will be prevented from taking any action other than appointing additional resident Canadian directors until such time as a sufficient number of new resident Canadian directors have been appointed such that at least 25% of the Company's directors are resident Canadians.

In addition, the Company does not carry key-man insurance on any individuals.

***The Company's employees and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could have a material adverse effect on the Company's business.***

The Company is exposed to the risk of employee and consultant fraud or other misconduct. Misconduct by employees and consultants could include, but are not limited to the following: failure to comply with regulators, failure to provide accurate information, failure to comply with manufacturing standards the Company has established, jurisdictional healthcare fraud and abuse of laws and regulations, failure to report financial information or data accurately or disclose unauthorized activities. For example, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee and consultant misconduct could

also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to the Company's reputation. If any such actions are instituted against the Company, and the Company is not successful in defending itself or asserting its rights, those actions could have a substantial impact on the Company's business and operating results, including the imposition of substantial fines, halt in trading of the Company's common shares, possible delisting and/or other sanctions.

***Indemnification obligations to directors and officers of the Company may adversely affect the Company's finances***

The Company has entered into agreements pursuant to which the Company has agreed to indemnify its directors and senior management in respect of certain claims made against them while acting in their capacity as such. If the Company is called upon to perform its indemnity obligations, its finances may be adversely affected.

***The Company's finances may fluctuate based on foreign currency exchange rates***

The Company operates internationally and is exposed to foreign exchange risks from various currencies, primarily the U.S. dollar, the Euro and the Polish Zloty.

***Unanticipated changes in the Company's tax rates could affect its future results***

Since the Company operates in different countries and is subject to taxation in different jurisdictions, its future effective tax rates could be impacted by changes in such countries' tax laws or their interpretations. Both domestic and international tax laws are subject to change as a result of changes in fiscal policy, changes in legislation, evolution of regulation and court rulings. The application of these tax laws and related regulations is subject to legal and factual interpretation, judgment and uncertainty.

***Shareholders of the Company may face dilution through exercise of stock options, warrants and future equity financings***

To attract and retain key personnel, the Company has granted options to its key employees, directors and consultants to purchase common shares and share awards as non-cash incentives. In addition, the Company has a significant number of warrants to purchase common shares outstanding. The issuance of shares pursuant to share awards and the exercise of a significant number of such options and warrants may result in significant dilution of other shareholders of the Company.

As noted above, the Company needs additional funding and has historically turned to the equity markets to raise this funding. The future sale of equity and warrants may also result in significant dilution to the shareholders of the Company.

***The Company's share price and trading volumes are volatile and the Company may have difficulty maintaining listing requirements***

The price of the Company's common shares, as well as market prices for securities of biopharmaceutical and drug delivery companies generally, have historically been highly volatile, and have from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies.

The trading price of the Company's common shares is subject to change and could in the future fluctuate significantly. The fluctuations could be in response to numerous factors beyond the Company's control, including: quarterly variations in results of operations; announcements of technological innovations or new products by the Company, its customers or competitors; changes in securities analysts' recommendations; announcements of acquisitions; changes in earnings estimates made by independent analysts; general fluctuations in the stock market; or revenue and results of operations below the expectations of public market securities analysts or investors. Any of these could result in a sharp decline in the market price of the common shares.

The Internet offers various avenues for the dissemination of information. The Company has no control over the information that is distributed and discussed on electronic bulletin boards and investment chat rooms. The intention of the people or organizations that distribute such information may not be in the Company's best interest and the best interests of its shareholders. This, in addition to other forms of investment information including newsletters and research publications, could result in a sharp decline in the market price of the common shares.

In addition, stock markets have occasionally experienced extreme price and volume fluctuations. The market prices for high-technology companies have been particularly affected by these market fluctuations and such effects have often been unrelated to the operating performance of such companies. These broad market fluctuations may cause a decline in the market price of the common shares.

Sales of substantial numbers of the Company's common shares could cause a decline in the market price of such common shares. There are minimum listing requirements for an issuer to maintain its listing on the Toronto Stock

Exchange (“TSX”), and if the Company fails to maintain these listing requirements, it may be involuntarily delisted from the TSX. De-listing the Company or the Company shares from any securities exchange could have a negative effect on the liquidity of the Company shares and/or the ability of a shareholder to trade in shares of the Company, and could have an adverse effect on the Company’s ability to raise future equity financings. The Company’s common shares trade in a very low volume compared to the number of common shares outstanding. This means a shareholder could have difficulty disposing of common shares, especially if there are other shareholders of the Company trying to sell their shares in the Company at the same time. Volatility in share price and trading volumes could have an adverse effect on the Company’s ability to raise future equity financings.

***The requirements of being a public company may strain the Company’s resources, divert management’s attention and affect its ability to attract and retain qualified board members***

As a public company, the Company is subject to the reporting requirements of Canadian securities regulators, the listing requirements of the Exchange and other applicable securities rules and regulations. Compliance with these rules and regulations may increase the Company’s legal and financial compliance costs, may make some activities more difficult, time-consuming or costly and may increase the demand on the Company’s systems and resources. Being a public company requires that the Company file continuous disclosure documents, including, among other things, annual and quarterly financial statements. Management’s attention may be diverted from other business concerns, which could have a material adverse effect on the Company’s business, financial condition and results of operations. The Company may need to hire more employees in the future, which will increase its costs and expenses.

In addition, changing laws, regulations and standards relating to corporate governance and public disclosure create uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. The Company may invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management’s time and attention from revenue-generating activities to compliance activities. If the Company’s efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory authorities, legal proceedings may be initiated against the Company and its business may be harmed.

***Trading in the Company’s common shares outside of Canada may be subject to restrictions on trading under foreign securities laws, and purchasers of securities under private placements by the Company will be subject to certain restrictions on trading***

The Company’s common shares trade on the TSX and are freely tradeable only in Canada. As such, shareholders trading the Company’s common shares outside of Canada may be subject to restrictions imposed by foreign securities laws that may restrict their ability to transfer shares freely or at all. Certain securities offered by the Company pursuant to its private placements, including the unlisted warrants issued by the Company, are subject to certain initial hold periods and other restrictions on trading imposed by applicable securities laws and, in the case of the warrants, pursuant to the terms of the applicable warrant certificates. These restrictions may affect the liquidity of the investment of certain shareholders in the securities of the Company.

***General economic conditions may have an adverse effect on the Company and its business***

Continuing global economic volatility and uncertainty may have an adverse effect on the Company and its business, including without limitation the ability to raise additional financing, to obtain strategic partner support or commercialization opportunities and alliances for the Company’s new drug candidates, and to obtain continued services and supplies.

***The Company’s business involves environmental risks that could result in accidental contamination, injury, and significant capital expenditures in order to comply with environmental laws and regulations***

The Company and its commercial collaborators are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of materials and certain waste products. Although the Company believes that its safety procedures comply with the regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. In the event of such an accident, the Company could be held liable for any damages that result and any such liability could exceed the resources of the Company. The Company is not specifically insured with respect to this liability. The Company (or its collaborators) may be required to incur significant costs to comply with environmental laws and regulations in the future; and the operations, business or assets of the Company may be materially adversely affected by current or future environmental laws or regulations.

***Any failure to maintain an effective system of internal controls may result in material misstatements of our consolidated financial statements or cause us to fail to meet our reporting obligations or fail to prevent fraud; and in that case, our shareholders could lose confidence in our financial reporting, which would harm our business, could negatively impact the price of our common shares and prevent the Company from raising additional capital.***

Effective internal controls are necessary for the Company to provide reliable financial reports and prevent fraud. If the Company fails to maintain an effective system of internal controls, the Company may not be able to report its financial results accurately or prevent fraud; and in that case, the Company's shareholders could lose confidence in our financial reporting, which would harm our business, negatively impact the price of the Company's common shares and also prevent the Company from raising additional capital. Even if we were to conclude that our internal control over financial reporting provides reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with IFRS as issued by the IASB, because of its inherent limitations, internal control over financial reporting may not prevent or detect fraud or misstatements. Failure to achieve and maintain effective internal control over financial reporting could prevent the Company from complying with its reporting obligations on a timely basis, which could result in the loss of investor confidence in the reliability of the Company's consolidated financial statements, harm our business, negatively impact the trading price of our common shares and prevent the Company from raising additional capital.

## **RISK FACTORS IN OTHER PUBLIC FILINGS**

For all of the reasons set forth above, together with those additional risk factors identified under the headings "*Forward-Looking Statements*" and "*Risk Factors*" in the Company's most recent Annual Information Form filed under the Company's profile on SEDAR at [www.sedar.com](http://www.sedar.com), investors should not place undue reliance on forward-looking information. Other than any obligation to disclose material information under applicable securities laws, the Company undertakes no obligation to revise or update any forward-looking information after the date hereof.

Data relevant to estimated market sizes and penetration for the Company's lead products under development are presented in this MD&A. This data has been obtained from a variety of published resources including published scientific literature, websites and information generally available through publicized means. The Company attempts to source reference data from multiple sources whenever possible for confirmatory purposes. Although the Company believes the foregoing data is reliable, the Company has not independently verified the accuracy and completeness of this data.

## **ADDITIONAL INFORMATION**

Additional information relating to the Company's fiscal year ended July 31, 2017, is available under the Company's profile on SEDAR at [www.sedar.com](http://www.sedar.com).

December 12, 2017