ANNUAL INFORMATION FORM

December 8, 2021

HELIX BIOPHARMA CORP.
9120 Leslie Street, Suite 205
Richmond Hill, Ontario, L4B 3J9

Tel: (905) 841-2300
Fax: (905) 841-2244
Web: www.helixbiopharma.com

TABLE OF CONTENTS

Page

FORWARD-LOOKING STATEMENTS

This annual information form ("AIF") contains "forward-looking statements" and "forward-looking information" within the meaning of applicable Canadian securities laws (collectively, "forward-looking information"). 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's primary drug product candidate L-DOS47 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, the extension of the current drug candidate(s) to other indications and the identification and development of further tumour-targeting antibodies for DOS47; (v) the nature, design and anticipated timeline for completion of enrollment and other matters relating to the Company's ongoing clinical study programs such as the Investigational New Drug ("IND") Phase Ib/II combination study combination with doxorubicin for previously treated advanced pancreatic cancer patients by the U.S Food and Drug Administration ("FDA"); (vi) the Company's seeking of strategic partner support and therapeutic market opportunities; (vii) future expenditures, insufficiency of the Company's current cash resources and the need for financing and the Company's possible response for such matters; (viii) future financing requirements, the seeking of additional funding and anticipated future operating losses; (ix) future evaluation and changes to the Company's disclosure controls and procedures related to internal controls over financial reporting and informing the public of such changes; (x) 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; (xi) the Company's technology and research and development objectives, including development milestones, estimated costs, schedules for completion and probability of success; (xii) the Company's expectation that it can in a timely manner, or at all, produce the appropriate preclinical, and if necessary, clinical data required; (xiii) the Company's plans to develop L-DOS47 and the estimated incremental costs (including the status, cost and timing of achieving the development milestones disclosed herein); (xiv) the Company's intentions with respect to initiating marketing activities following receipt of the applicable regulatory approvals; (xv) the Company's seeking of licensing opportunities to expand its intellectual property portfolio; (xvi) the Company's expectation that it will be able to finance its continuing operations by accessing public markets for its securities; (xvii) the Company's intended use of proceeds of any offering of its securities; and (xviii) the Company's intention with respect to not paying any cash dividends on its common shares in the capital of the Company ("Common Shares") in the foreseeable future. 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", "2021", "2022", "2023", "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 AIF as a result of numerous known and unknown risks and uncertainties, including, but not limited to:

- the Company's lack of operating income and need for additional capital which may not be available in a timely manner or at all;
- the Company's history of losses and expectations regarding incurring additional losses for the foreseeable future;
- rapid technological change and competition from pharmaceutical companies, biotechnology companies and universities, which may make the Company's technology or products obsolete or uncompetitive;
- the Company's dependence on a drug platform with only a single drug product candidate, L-DOS47 currently in clinical trials. uncertainty as to the size and existence of a market opportunity for, and market acceptance of the Company's drug product candidate 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;
- the possibility that the market may never accept L-DOS47 or any other drug product candidate from the Company's DOS47 platform technology;

- uncertainty as to product development milestones and, in particular, whether the Company's drug product candidate(s), especially L-DOS47, will be successfully developed and marketed;
- 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 confidential proprietary information;
- risks relating to patent litigation;
- risks relating to security breaches and other disruptions which may compromise the Company's information and expose the Company to liability and cause the Company's business and reputation to suffer;
- risks related to the potential infringement by the Company of the intellectual property rights of third parties, and the possibility that such parties may commence legal proceedings to protect or enforce such rights, the outcome of which would be uncertain and could harm the Company's business;
- risks associated with claims, or potential claims, of infringement of third-party intellectual property and other proprietary rights;
- risks relating to lawsuits or other proceedings commenced by the Company to protect or enforce the Company's patents or other intellectual property, and their potential effect on the Company;
- risks relating to potential claims of third parties that the Company's employees, collaborators, consultants or independent contractors have wrongfully used or disclosed the confidential information of third parties, or that the Company's employees have wrongfully used or disclosed alleged trade secrets of their former employers;
- 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;
- regulatory risks, including the lengthy, unpredictable and costly FDA regulatory approval process and the potential impact on the Company if such approvals are not ultimately obtained;
- the risk of unknown side effects arising from the development, manufacture or use of the Company's products;
- risk relating to the difficulty in enrolling patients in clinical trials which may result in delays or cancellation of clinical trials;
- 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 significant dependence on licensed intellectual property and the risk of losing or breaching such licenses;
- 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;
- risks relating to the marketability of the Company's products arising from regulatory delays or inability to obtain regulatory approval, and ongoing regulatory review and requirements;
- 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);
- 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;
- risks relating to the Company's potential failure to find third party collaborators to assist or share in the costs of product development and the potential impact on the Company's business, financial condition and results of operations;
- the need for future preclinical and clinical trials, and the reliance by the Company on third parties to conduct such 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;
- product liability and insurance risks;
- the risk of lawsuits and other legal proceedings against the Company;
- uncertainty as to the Company's ability to maintain product liability insurance required by third parties and the risk of the corresponding agreement being terminated;
- the need to attract and retain key personnel and reliance on key personnel;

- the risk of misconduct on the part of employees and consultants, including non-compliance with regulatory standards and requirements;
- the risk that indemnification obligations to directors and officers may adversely affect the Company's finances;
- the impact on the Company's finances resulting from shifts in foreign exchange rates, credit risk and interest rate risk;
- risks related to adverse decisions by tax authorities and changes in law;
- risks relating to the potential financial strain on the Company's resources due to the requirements of being a public company;
- the impact of the ongoing volatility in the economic environment;
- risks relating to compliance with environmental laws;
- risk relating to a failure to maintain an effective system of internal controls;
- risks related to epidemics, pandemics or other health crises, including the coronavirus ("COVID-19") pandemic, and their potential effect on the Company's business, operations and financial condition;
- volatility in the trading price and volume of the Common Shares and potential challenges in maintaining listing requirements;
- the possibility of dilution to current shareholders from future equity or convertible debt financings or through the exercise of stock options ("Options"), Common Share purchase warrants ("Warrants") or other securities convertible or exchangeable into Common Shares;
- liquidity of the Common Shares;
- the risk that inaccurate or unfavorable research about the Company's business, or the lack of research about its business, may affect the share price and trading volume of the Common Shares;

and other risk factors that are discussed above and elsewhere in this AIF or identified in the Company's other public filings under the Company's profile on SEDAR at www.sedar.com (collectively, the "Helix Risk Factors"), any of which could cause actual results to vary materially from current results or the Company's anticipated future results. Forward-looking information in this AIF is based on certain material factors, estimates or assumptions, which may prove to be incorrect, including, but not limited to assumptions about: general business and current global economic conditions; future success of current research and development activities; achievement of development milestones; inability to achieve product cost targets; competition; changes to tax rates and benefits; the availability of financing on a timely basis; the Company's and its competitors' costs of production and operations; the Company's ability to attract and retain skilled employees; receipt of all applicable regulatory approvals/clearances; protection of the Company's intellectual property rights; market acceptance of the Company's product candidates; the Company's ability to meet the continued listing requirements of the Toronto Stock Exchange ("TSX"); and that the Helix Risk Factors will not cause the Company's actual results or events to differ materially from the forward-looking information. The Company cautions that the foregoing list of important factors and assumptions is not exhaustive.

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 AIF. 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.

CORPORATE STRUCTURE

Name, address and incorporation

Helix BioPharma Corp. ("**Helix**" or the "**Company**") is a Canadian corporation which was originally formed upon the amalgamation of International Helix Biotechnologies Inc. and Intercon Pharma Inc. on July 31, 1995. On April 30, 2008, the Company further amalgamated under the *Canada Business Corporations Act* with Helix Product Developments Inc., 6933912 Canada Ltd., Sensium Technologies Inc. and 6965954 Canada Inc.

The Company`s principal corporate office is located at 9120 Leslie Street, Suite 205, Richmond Hill, Ontario, Canada L4B 3J9. The Company`s phone number is (905) 841-2300. The Company`s website is www.helixbiopharma.com.

Inter-corporate relationships

During the year ended July 31, 2021, Helix Immuno-Oncology S.A. ("HIO"), the Company's only existing subsidiary which was incorporated in Poland on July 6, 2013, completed a direct financing with an arm's length party on September

3, 2020. As a result of the financing the Company's ownership in HIO was diluted down to 29.89% and as a result, the Company determined that it has lost control of HIO. On November 9, 2020, the Company announced that it had signed a definitive share purchase agreement with CAIAC Fund Management AG ("CAIAC"), as designated trustee of HIO Fund (the "Fund"), to purchase the Company's remaining holdings in HIO for gross proceeds of PLN 6,700,000 ($2,308,000) (the "HIO Disposition"). The HIO Disposition closed on December 22, 2020.

There were no material amendments to the Company`s articles or other constating documents in the 2021 fiscal year.

GENERAL DEVELOPMENT OF THE BUSINESS

Helix is a clinical-stage biopharmaceutical company developing unique therapies in the field of immuno-oncology for the prevention and treatment of cancer based the Company's proprietary technological platform DOS47. The Company's product development initiatives are focused primarily on technologies that modulate the tumour microenvironment.

Important events which have occurred in the last three fiscal years and the period subsequent to July 31, 2021 up to the date of filing this AIF under the Company's profile on SEDAR at www.sedar.com include the following:

July 31, 2021 to the date of this AIF

- On November 30, 2021, the Company announced a further delay in the filing of its annual consolidated financial statements, management's discussion and analysis, annual information form and related officer certifications for the financial year ended July 31, 2021 (the "Annual Documents"), with a revised target date for filing of December 10, 2021;

- On November 15, 2021, the Company announced a further delay in the filing of its annual consolidated financial statements, management's discussion and analysis, annual information form and related officer certifications for the financial year ended July 31, 2021 (the "Annual Documents"), with a revised target date for filing of December 3, 2021;

- On November 1, 2021, the Company announced that it had been granted a management cease trade order (the "MCTO") by the Ontario Securities Commission (the "OSC") in connection with the previously announced delay in the filing of its Annual Documents, which Annual Documents it also announced it expected to file by November 19, 2021.

- On October 15, 2021, the Company announced that there would be a delay in the filing of the Annual Documents and that it had made an made an application to the OSC, as principal regulator of the Company, for an MCTO under National Policy 12-203 in respect of the anticipated default regarding the delayed filing of the Annual Documents.

- On September 20, 2021, the Company announced the appointment of the company's Chairman, Dr. Slawomir Majewski, as Interim Chief Executive Officer to hold office while the Board worked to identify and evaluate potential candidates as permanent Chief Executive Officer ("CEO").

- On August 19, 2021, the Company announced that Dr. Krzysztof Saczek has been appointed as a member of the Board effective immediately in connection with the resignation of Heman Chao as CEO and as a director of the Company.

Fiscal year ended July 31, 2021

- On June 30, 2021, the Company announced that Heman Chao had notified the Board of his intention to step down from the position of CEO and Chief Scientific Officer and member of the Board, effective September 1, 2021, on which date Mr. Chao assumed the position of Chair of the Company's Scientific Advisory Board.

- On May 10, 2021, the Company entered into a definitive convertible security funding agreement (the "Lind Agreement") with Lind Global Macro Fund, LP, a New York based institutional investment fund managed by The Lind Partners, LLC ("Lind"). The Company closed the first tranche ("First Tranche") under the Lind Agreement on May 13, 2021, for gross proceeds of $3,500,000. In connection with the closing of the First Tranche, the Company issued a convertible security (a "Convertible Security") of the Company with a two-year term and a face value of $4,112,500 and issued an aggregate of 1,957,056 Warrants exercisable into Common Shares until May 13, 2023, at an exercise price of $1.0283 per Common Share. In connection with the closing of the First Tranche, the Company paid Lind a 3% commitment fee of the amount funded under the First Tranche. The Lind Agreement contemplates the issuance of a second Convertible Security subject

to certain conditions precedent and upon the mutual agreement of the Company and Lind for gross proceeds to the Company of up to $6,500,000.

- On December 30, 2020, the Company announced it had closed a private placement financing of units of the Company for gross proceeds of $3,000,000 at a price of $0.50 per unit. Each such unit was comprised of one Common Share and one Warrant entitling the holder thereof to purchase one Common Share at an exercise price of $0.70 for a period of five years from the date of issuance.

- On December 4, 2020, the Company announced it had closed a private placement financing of units of the Company for gross proceeds of $1,100,000 at a price of $0.50 per unit. Each such unit was comprised of one Common Share and one Warrant entitling the holder thereof to purchase one Common Share at an exercise price of $0.70 for a period of five years from the date of issuance.

- On October 29, 2020, the Company announced that, effective October 21, 2020, the financial advisory services agreement dated July 2, 2018 between the Company and ACM Consulting Management AG and the investor relations and advisory services agreement dated July 2, 2018 between the Company and ACM Consulting Management Est. had been terminated by the mutual agreement of the parties.

- On September 3, 2020, HIO completed a direct financing with an arm's length party. As a result of the financing the Company's ownership in HIO was diluted down to 29.89% and as a result, the Company determined that it had lost control of HIO from an accounting perspective. On November 9, 2020, the Company announced that it had signed a definitive share purchase agreement with CAIAC, as designated trustee of the Fund, to purchase the Company's remaining holdings in HIO for gross proceeds of PLN 6,700,000 ($2,308,000).The HIO Disposition closed on December 22, 2020.

- On August 28, 2020, CAIAC, as portfolio manager for Biotech Opportunity Fund, announced that it acquired control and/or direction over 26,363,172 Common Shares for aggregate consideration of approximately $13.18 million and, as a result of the transaction, CAIAC exercised control and/or direction over, and Biotech Opportunity Fund owned, approximately 19.83% of the Company's issued and outstanding Common Shares on a non-diluted basis.

- On August 12, 2020, the Company announced that it had extended its collaboration agreement with Moffitt Cancer Center for an additional year to provide additional preclinical support in using L-DOS47 with immunotherapies as clinical support.

Fiscal year ended July 31, 2020

- On June 26, 2020, the Company announced that it had approved, in its capacity as a shareholder of HIO, a direct investment in HIO by an investor which resulted in the Company's ownership in HIO being reduced to approximately 42.5% on July 8, 2020. The direct investment in HIO permitted HIO to apply for a new government grant for the development of the multiple myeloma CAR-T program in Poland.

- On June 26, 2020 the Company announced the receipt of a non-binding offer from CAIAC, as designated trustee of an alternative investment fund to be established, to purchase the Company's remaining shares in HIO. The transaction which was originally expected to close on August 31, 2020, subject to the satisfaction of certain conditions, including, but not limited to, the negotiation of binding documentation, the receipt of a minimum of PLN7,300,000 ($2,377,026) by CAIAC pursuant to a financing, and the receipt of all required regulatory approvals. The HIO Disposition closed on December 22, 2020.

- On June 26, 2020, the Company announced the cancellation of intercompany debt in the total aggregate amount of approximately $2,700,000 owed to the Company by HIO. As part of the debt cancellation, both the V-DOS47 and Biphasix™ agreements between the Company and HIO were terminated with immediate effect.

- On May 14, 2020, the Company announced that topline data of the L-DOS47 dose escalation study in combination with pemetrexed and carboplatin in recurrent or metastatic non-squamous non-small cell lung cancer would be published at the ASCO 2020 Annual Conference.

- On March 12, 2020, the Company announced the closing of a private placement of units of the Company and the disposition of a 15.5% stake in HIO, for gross proceeds of approximately $6,000,000. The transaction resulted in the Company's ownership of HIO being reduced to approximately 51%.

- On January 30, 2020, HIO conveyed to the Polish National Centre for Research and Development ("PNCRD") that it wished to terminate the grant funding program for V-DOS47.

- On January 13, 2020, the Company announced the closing of a private placement of units of the Company and the disposition of an 8.5% stake in HIO, for gross proceeds of approximately $3,000,000. The transaction resulted in the Company's ownership of HIO being reduced to approximately 66.5%.

- On December 6, 2019, at the Company's annual and special meeting of shareholders, Messrs. Artur Gabor, Ireneusz Fąfara, Slawomir Majewski and Heman Chao were elected to the Board by shareholders. The approval to an amendment to the articles of the Company to consolidate the issued and outstanding Common Shares, as and when determined by the Board, was also obtained.

- In December 2019, the Company announced the start of enrollment and screening for its Phase Ib/II clinical development program for previously treated patients with advanced pancreatic cancer. The study center is located in Scottsdale, Arizona at the Scottsdale Hospital ("HonorHealth").

- On October 10, 2019, the Company announced that the Board accepted the resignation of Mr. Sylwester Cacek as a director of the Company and that Mr. Ireneusz Fąfara had been appointed to the Board in his place, effective October 9, 2019.

- On August 21, 2019, the Company announced the closing of a private placement of units of the Company and the disposition of a 25% stake in HIO, for gross proceeds of approximately $7,000,000. Mr. Jerzy Wilczewski acquired all of the 13,725,500 units sold pursuant to the private placement. The Company obtained disinterested shareholder approval at its annual and special meeting of shareholders held on December 6, 2019 for the potential creation of Mr. Wilczewski as a "control person" resulting from the exercise of all or a portion of the Warrants held by him.

- On August 7, 2019, the Company announced the approval of the FDA to initiate a Phase Ib/II study of L-DOS47 and doxorubicin in patients with previously treated advanced pancreatic cancer.

Fiscal year ended July 31, 2019

- On July 9, 2019, the Company announced the submission of an L-DOS47 investigational new drug application with the U.S. FDA for a phase 1/2 clinical study protocol with L-DOS47, to be given in combination with doxorubicin, for the treatment of metastatic pancreatic cancer.

- On May 30, 2019, the Company announced the commencement of the process to have the Company's Common Shares quoted on the OTCQB® Market exchange in the United States and the retention of Alpha Bronze LLC to act as investor relations agent.

- On May 29, 2019, the Company announced the closing of a private placement for gross proceeds of approximately $500,000.

- On April 30, 2019, the Company announced that the Trial Steering Committee ("TSC") reviewed safety data from the first dosing cohort of the Company's LDOS003 study, no serious adverse events or dose limited toxicities were observed, and that the TSC recommended that the Company begin enrollment of patients into the second dosing cohort.

- On April 18 and April 29, 2019, the Company announced the closing of a private placement for gross proceeds of approximately $1,500,000.

- On April 17, 2019, the Company announced the retention of Sheppard Mullin, Richter and Hampton LLC as its U.S. legal counsel and the retention of RHK Capital to advise on U.S. listing alternatives.

- On April 15, 2019, at the Company's annual and special meeting of shareholders, Messrs. Sylwester Cacek, Artur Gabor, Slawomir Majewski and Heman Chao were elected to the Board by shareholders. In addition, disinterested shareholder approval of the extension of the expiry date of 3,862,000 Warrants held by insiders by a period of two years and shareholder approval to an amendment to the articles of the Company to consolidate the issued and outstanding Common Shares, as and when determined by the Board, was obtained.

- On March 15, 2019, the Company announced the closing of a private placement for gross proceeds of approximately $600,000. The Company also announced the conditional approval of the TSX to extend the maturity of 12,661,000 outstanding Warrants, for a period of two years, of which 8,799,999 Warrants held by arms' length parties were extended effective March 29, 2019, and 3,862,000 Warrants held by insiders, were to be extended on the date that disinterested shareholder approval was obtained. Following the extension of the Warrants, the expiry dates of the Warrants ranged from July 9, 2021 to April 28, 2022. The exercise prices of the Warrants ranging from $1.54 to $2.24 remained unchanged.

- On March 7, 2019 the Company announced the successful dosing of the first patient with L-DOS47, vinorelbine and cisplatin in its Phase IIB, open label, randomized study in metastatic lung adenocarcinoma patients.

- On February 27, 2019, the Company announced, together with Moffitt Cancer Center, the presentation of a poster entitled "Improving survival in pancreatic cancer using Doxorubicin in combination with L-DOS47" at the American Association for Cancer Research Annual Meeting 2019 on March 29-April 3, 2019 in Atlanta, Georgia, USA.

- On February 11, 2019, the Company announced the extension of its collaboration with Moffitt Cancer Center, an expecting filing of an IND application with the FDA for an L-DOS47 pancreatic cancer study in combination with doxorubicin and the consideration of a new L-DOS47 combination study with pemetrexed, cisplatin and immunotherapy, such as Keytruda®. In addition, the Company announced discussions regarding the divesture of a majority stake in its wholly owned Polish subsidiary, discussions with several U.S. based financial advisory firms and its attendance at BIO CEO Conference in New York.

- On December 6, 20, 21 and 28, 2018, the Company announced the closing of a private placement for aggreate gross proceeds of approximately $2,260,000.

- On November 13, 2018, the Company provided a strategic update of its active L-DOS47 clinical program and its strategic plan for L-DOS47.

- On November 1, 2018, the Company announced the initiation of a new clinical program in pancreatic cancer, led by Dr. Daniel D. Von Hoff.

- On October 30, 2018, the Company announced the closing of a private placement for gross proceeds of approximately $340,000.

- On October 16, 2018, the Company announced the conditional approval by the TSX to extend the maturity of 4,546,000 outstanding Warrants, all of which were held by arm's-length parties, by a period of two years, to October 31, 2020. The exercise price of the warrants remained unchanged at $1.61, and the effective date of the amendment was October 31, 2018.

- On October 10, 2018, the Company announced the extension of its collaboration agreement with the Moffitt Cancer Centre for an additional year.

- On September 13, 2018, the Company announced the initiation of enrollment of the second to last cohort in the U.S. combination treatment study of L-DOS47.

- On September 12, 2018, the Company announced that a scientific research collaborator published a paper describing research and validation work on the antibody that the companies are co-developing for a CAR-T application against multiple myeloma.

- On September 10, 2018, the Company announced the closing of a private placement for gross proceeds of approximately $0.46 million.

- On August 8, 2018, the Company announced the closing of a private placement for gross proceeds of approximately $0.82 million.

DESCRIPTION OF THE BUSINESS

Overview

Helix is a clinical-stage biopharmaceutical company developing unique therapies in the field of immuno-oncology for the prevention and treatment of cancer based on its proprietary technological platform DOS47.

The Company is pioneering the development of a platform technology targeting the tumour microenvironment. Helix's technology is designed to reduce tumour acidity, an escape mechanism which cancer cells utilize to evade the anti-tumour immune response. Tumour acidity has been shown to correlate with resistance to anti-cancer treatment and poor prognosis for cancer patients.

To date, the Company's proprietary technology platform, DOS47 has yielded two new drug product candidates, being L-DOS47 and V-DOS47.

L-DOS47 is currently under clinical study for the treatment of non-small cell lung cancer ("NSCLC") and previously treated advanced pancreatic cancer. The Company completed extensive preclinical testing and manufacturing development of L-DOS47, following which the Company obtained regulatory approvals to conduct a Phase I/II NSCLC monotherapy clinical study in Poland, a Phase I NSCLC combination study with pemetrexed and carboplatin in the United States, and a Phase II NSCLC combination study with vinorelbine and cisplatin in Ukraine and Poland. In August 2019, the Company also received approval to conduct a Phase Ib/II combination study utilizing L-DOS47 with doxorubicin in patients with previously treated advanced pancreatic cancer in the United States.

V-DOS47 drug candidate uses the Company's proprietary DOS47 technology conjugated to anti-VEGFR2 antibody targeting a wide range of cancers. In 2016, V-DOS47 was licensed to Helix Immuno-Oncology S.A., the Company's then wholly owned Polish subsidiary, ("HIO"), for pre-clinical and clinical development activity. HIO entered into a grant funding agreement with the Polish National Centre for Research and Development ("PNCRD") to fund the V-DOS47 research project. On January 30, 2020, HIO conveyed to the PNCRD that it wished to terminate the grant funding program for V-DOS47. Under the grant funding agreement, HIO received approximately $1,457,000. As part of the debt cancellation agreements announced by the Company on June 26, 2020, the Company and HIO terminated the V-DOS47 license agreement. As a result, all transferred assets related to V-DOS47 have been automatically reassigned and transferred from HIO back to the Company without any formality. As a result, the Company will now assess what next steps to take with the V-DOS47 antibody.

In NSCLC, L-DOS47 has shown to be safe and well tolerated as a monotherapy pursuant to the Company's LDOS002 study ("LDOS002"). L-DOS47 has also shown to be safe and well tolerated when used in combination with pemetrexed and carboplatin pursuant to the Company's LDOS001 study ("LDOS001"). LDOS001 was conducted at University Hospital's Case Medical Center in Cleveland, Ohio, at Penn State's Cancer Institute in Hershey, Pennsylvania and at the University of Texas MD Anderson Cancer Center in Houston, Texas. As reported at the June 2020 conference of the American Society of Clinical Oncology, an objective response rate of 41.7% based on tumour burden and a clinical benefit rate of 75% inclusive of stable diseases were observed in the LDOS001 study. The Company believes the data supports the continuing development of L-DOS47 for NSCLC. As of the date of this AIF, the Company is contemplating a new study in NSCLC using L-DOS47 in combination with immunotherapy and has hired several consultants to provide an assessment of the Company's technology and advise on clinical strategic priorities.

In December 2019, the Company announced the start of enrollment and screening for its Phase Ib/II clinical development program for previously treated patients with advanced pancreatic cancer. The study center is located in Scottsdale, Arizona at the Scottsdale Hospital (dba "HonorHealth"). The Company originally forecasted patient enrollment in the Phase Ib portion of the study to be completed by the end of the 2020 calendar year, pending safety outcomes and the impact of the COVID-19 pandemic. As a result of the COVID-19 pandemic, the Company has not met the previously forecasted patient enrollment timeline for this clinical study. The Company added two new clinical sites in other U.S. jurisdictions during the first quarter of 2021, in order to facilitate patient enrollment. The Company believes patient enrollment in the Phase Ib portion of the study may be completed by the second quarter of calendar year 2022. However, any cohort expansion in the dose escalation phase will result in a three-month extension in the projected timeline. Please see "Our results of operations may be negatively impacted by the COVID-19 outbreak" under the heading "Risk Factors".

In 2017, the Company entered into a scientific research collaboration agreement with the Moffitt Cancer Center ("Moffitt") in Tampa, Florida, to perform basic research studies to further investigate the pharmacodynamics of L-DOS47 and to determine the potential benefits of combining L-DOS47 with immune checkpoint inhibitors. The Company's collaboration with Moffitt continues while the Company assesses the possibility of expanding its collaboration with Moffitt. Pancreatic cancer is known to be a disease that is resistant to immunotherapy treatment and shown in animal models to be highly acidic. The Company believes the ability of L-DOS47 to modulate tumour acidity may be key to enable immunotherapy treatment for pancreatic cancer. This new research collaboration project will also build on data already obtained from imaging techniques performed by Moffitt that demonstrated the ability of L-DOS47 to affect tumour acidity. Translation of this technique into the clinic may help stratify patients for L-DOS47 and potentially identify patients who may be resistant to certain therapies due to tumour acidity.

In addition to DOS47, the Company has also developed antibodies that may be suitable for novel chimeric antigen receptor T-Cell therapeutic ("CAR-T") for solid tumours. In March 2018, the Company announced a scientific research collaboration with ProMab Biotechnologies Inc. ("ProMab") to co-develop Car-T that target BCMA to treat multiple myeloma. In this collaboration, the Company retains commercial rights for this CAR-T in Canada and Europe. The Company entered into a sublicense agreement for BCMA with HIO whereby the Company will assist in preclinical and early phase clinical planning of the BCMA project. The Company's assistance includes funding a certain portion(s) of the preclinical development stage while HIO leads the regulatory and clinical development of the product in Europe. The Company fulfilled its obligation regarding this collaboration agreement during fiscal 2021. These activities are expected to be coordinated with ProMab who will be developing the product for Asia and the U.S. The Company retains the rights for Canada.

In December 2016, the Company 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. Under the terms of the agreement, Xisle paid an up-front fee and agreed to pay subsequent milestone payments and royalties to the Company as Xisle advances the technology. As part of the agreement, the Company retained marketing rights for Belarus, Bulgaria, the Czech Republic, former Eastern Germany, Hungary, Moldova, Poland, Romania, Russia, Slovakia and Ukraine and non-exclusive rights for co-promotion in Canada. The Company subsequently assigned the foregoing marketing rights which it retained to HIO pursuant to an agreement between the Company and HIO, which terminated on June 26, 2020 in connection with the cancellation of intercompany debt owed by HIO to the Company.

On June 26, 2020, the Company announced that it had approved, in its capacity as a shareholder of HIO, a direct investment in HIO by an investor which resulted in the Company's ownership in HIO being reduced to approximately 42.51% on July 8, 2020. The direct investment in HIO permitted HIO to apply for a new government grant for the development of the multiple myeloma CAR-T program in Poland. On September 3, 2020, HIO closed another direct private placement with an arm's length party, CAIAC Fund Management AG ("CAIAC"), as designated trustee of an alternative investment fund to be established, resulting in a further dilution of the Company's holding in HIO from 42.51% as at July 31, 2020 down to 29.89%.As a result of the financing, the Company's ownership in HIO was diluted down to 29.89% and consequently, the Company has determined that it had lost control of HIO. During the year ended July 31, 2021, the Company received gross cash consideration of PLN 6,700,000 (CAD$2,308,000) for the balance of its shares in HIO ($2,020,000 net of costs of disposition), resulting in the full disposition of its interest in the associate.

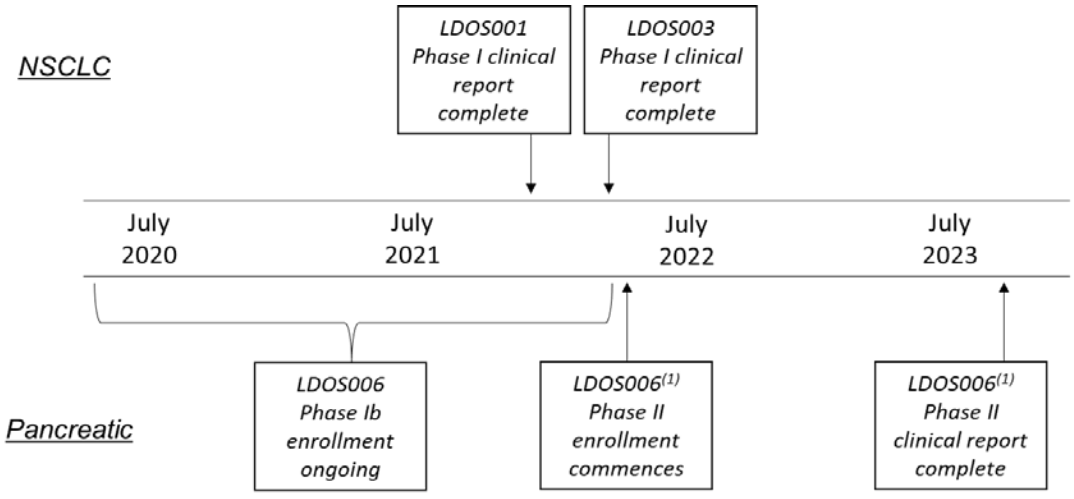
Also on June 26, 2020, the Company also announced the cancellation of intercompany debt in the total aggregate amount of approximately $2,700,000 owed to the Company by HIO. As part of the debt cancellation, both the V-DOS47 and Biphasix™ agreements between the Company and HIO described above were terminated with immediate effect.

The Company has an extensive patent portfolio that includes company owned and licensed patents and pending applications, including, but not limited to, the use of DOS47 as immunoconjugate for cancer treatment. The Company also has licenses with the National Research Council of Canada ("NRC") that cover the use of antibodies for L-DOS47, other DOS47 candidates and cellular therapy products. Issued patents have coverage in all major pharmaceutical markets including North America, Europe, and Asia.

The Company currently believes that its growth and future prospects are mainly dependent on the success of its DOS47 drug product candidates.

Product focus and strategy

The Company is currently focused on the development, commercialization &/or partnership of L-DOS47 as a potential therapy for NSCLC and pancreatic cancer but at the same time is evaluating the current clinical strategy to determine if the Company's L-DOS47 pipeline can be expanded into other indications. The following diagram sets forth the status and milestones related to the Company's current L-DOS47 clinical program.



1) subject to successfully achieving Phase Ib protocol requirements and availability of sufficient financing

NSCLC

- Completion of the LDOS001 Phase I LDOS-47 pemetrexed/carboplatin combination study clinical report by December 2021.

- Completion of the LDOS003 Phase I LDOS-47 vinorelbine/cisplatin combination study clinical report in March 2022.

Pancreatic

- Completion of the LDOS006 Phase Ib doxorubicin combination study has been pushed out to March 2022. COVID-19 in 2020 materially hindered patient enrollment resulting in the Company adding two new clinical sites early in calendar year 2021. The clinical study was also impacted with two adverse events which resulted in the expansion of the number of patients previously forecasted to complete the Phase Ib portion of the study.

- Provided the LDOS006 Phase Ib portion of the study is successfully completed, the Company is forecasting patient enrollment for the Phase II portion of the study to commence no later than June 2022 with a final clinical report by September 2023. Unlike the Phase Ib study where new patient enrollment must be completed sequentially, the Phase II portion of the study allows for multiple patient enrollment simultaneously which could reduce the currently projected timeline.

A different approach – targeting the acidic tumor microenvironment

The pH system, with values ranging from 0 – 14, is used to measure acidity (pH < 7) and alkalinity (pH > 7). In general, the human body exists at a near-neutral pH - neither acidic nor alkaline (basic). In order for cells to function properly, they need the pH both inside and outside the cell to be neutral. There are some examples, however, where this rule is not followed. For example, the inside of the stomach is maintained at an acidic pH, as this helps to digest food. The cells lining the stomach have adapted to live in this acidic environment[1].

Tumors also exist in an acidic environment. Normal tissues include an extensive network of blood vessels, which deliver oxygen and nutrients to cells and remove waste products. However, tumors contain an abnormal network of blood vessels. Because of this, tumors are hypoxic (receive less oxygen than normal tissues) and need to use a non-oxygen requiring form of metabolism to provide energy for their survival and growth. One side-effect of this type of metabolism is that it generates an excess of hydrogen ions (H^+) inside the cell, and hydrogen ions directly affect pH: the more hydrogen ions there are, the more acidic the inside of the cell becomes. Since a neutral pH inside the cell is essential for a cell to survive, tumor cells pump the excess hydrogen ions out of the cell. Due to the abnormal network of blood vessels, the excess hydrogen ions are not efficiently removed from the tumor microenvironment. Thus, the tumor microenvironment is acidic[2].

The acidic microenvironment helps promote tumor survival and metastasis in a number of ways. The genes expressed by the tumor are affected by the acidic microenvironment, which allows tumor cells to adapt[3]. One of these acid-induced changes is to increase production and release of proteases by tumor cells[4,5]. The proteases destroy the protein matrix that surrounds the tumor cells, which makes it easier for the tumor cells to invade local tissues – a first step to metastasis. In addition, the acidic tumor microenvironment has been shown to impair the activity of immune cells in the tumor, which allows the tumor cells to avoid destruction by the immune system[6].

The acidic tumor microenvironment also reduces the efficacy of common cancer treatments. Some chemotherapy drugs, such as doxorubicin, are weakly basic. The ability of these drugs to enter tumor cells, where they perform their

[1] Hsu M, Lui F (2020) Physiology, Stomach. StatPearls. StatPearls Publishing. Copyright © 2020, StatPearls Publishing LLC., Treasure Island (FL)

[2] Kato Y, Ozawa S, Miyamoto C, Maehata Y, Suzuki A, Maeda T, Baba Y (2013) Acidic extracellular microenvironment and cancer. Cancer Cell Int. 13: 89. doi: 10.1186/1475-2867-13-89

[3] Chen JL, Lucas JE, Schroeder T, Mori S, Wu J, Nevins J, Dewhirst M, West M, Chi JT (2008) The genomic analysis of lactic acidosis and acidosis response in human cancers. PLoS Genet. 4: e1000293. doi: 10.1371/journal.pgen.1000293

[4] Glunde K, Guggino SE, Solaiyappan M, Pathak AP, Ichikawa Y, Bhujwalla ZM (2003) Extracellular acidification alters lysosomal trafficking in human breast cancer cells. Neoplasia. 5: 533-45. doi: 10.1016/s1476-5586(03)80037-4

[5] Rothberg JM, Bailey KM, Wojtkowiak JW et al. (2013) Acid-mediated tumor proteolysis: contribution of cysteine cathepsins. Neoplasia. 15: 1125-37. doi: 10.1593/neo.13946

[6] Lacroix R, Rozeman EA, Kreutz M, Renner K, Blank CU (2018) Targeting tumor-associated acidity in cancer immunotherapy. Cancer Immunol Immunother. 67: 1331-48. doi: 10.1007/s00262-018-2195-z

function, is greatly reduced at acidic pH compared to neutral pH[7]. Radiation therapy also is less effective at an acidic pH than at a neutral pH[8].

It is clear that the acidic tumor microenvironment has a profound effect both on tumor biology and current therapies, and that neutralizing the pH of the tumor microenvironment may have a dramatic impact. One way to reverse extracellular tumor acidity is to inhibit the proteins that pump hydrogen ions out of tumor cells[9]. One advantage of inhibiting these proteins is that not only is acidity of the extracellular tumor microenvironment reduced, but acidity inside the tumor cells increases, which has a negative effect on tumor cell viability. However, targeting these pumps is not easily achieved as many of them exist in multiple forms and some are critical for the function of normal cells[10]. In addition, since there are several different pumps that regulate pH, inhibition of just one is generally insufficient to combat tumor acidity.

A more general and theoretically more effective method to neutralize tumor extracellular pH is to use buffers. A variety of orally administered buffers have been effective in reducing tumor growth and/or metastases in preclinical animal studies[11,12,13,14]. In addition, buffer therapies have been shown to enhance the activities of chemotherapy and immunotherapy[15,16,17]. Although oral sodium bicarbonate buffer therapy was tested clinically, these trials failed due to poor compliance and moderate adverse effects[18]. However, improved survival was seen in pancreatic cancer patients undergoing chemotherapy and “alkalization therapy” (produced by changes in diet and consumption of bicarbonate)[19].

Similarly, an alkaline diet likely improved responses to epithelial growth factor receptor – tyrosine kinase inhibitor (EGFR-TKI) therapy in non-small cell lung cancer (NSCLC) patients[20]. Thus, a change in delivery method may allow for successful buffer therapy. Consistent with this hypothesis, administration of *iv* sodium bicarbonate nanoparticles improved doxorubicin efficacy in a preclinical breast cancer model[21]. In addition, a clinical study was performed in which sodium bicarbonate was administered by local infusion into the tumor. In this study, hepatocellular carcinoma patients were treated with trans-arterial chemoembolization (TACE) with or without local bicarbonate. Patients receiving bicarbonate showed a 6-fold lower viable tumor residue, and a randomized controlled study showed that patients treated with bicarbonate had a higher objective response rate and cumulative overall survival in comparison to the patients treated with TACE alone[22].

---

[7] Kolosenko I, Avnet S, Baldini N, Viklund J, De Milito A (2017) Therapeutic implications of tumor interstitial acidification. Semin Cancer Biol. 43: 119-33. doi: 10.1016/j.semcancer.2017.01.008

[8] Hunter A, Hendrikse A, Renan M, Abratt R (2006) Does the tumor microenvironment influence radiation-induced apoptosis? Apoptosis. 11: 1727-35. doi: 10.1007/s10495-006-9789-1

[9] Parks SK, Pouyssegur J (2017) Targeting pH regulating proteins for cancer therapy-Progress and limitations. Semin Cancer Biol. 43: 66-73. doi: 10.1016/j.semcancer.2017.01.007

[10] Supuran CT (2008) Carbonic anhydrases: novel therapeutic applications for inhibitors and activators. Nat Rev Drug Discov. 7: 168-81. doi: 10.1038/nrd2467

[11] Ibrahim Hashim A, Cornnell HH, Coelho Ribeiro Mde L, Abrahams D, Cunningham J, Lloyd M, Martinez GV, Gatenby RA, Gillies RJ (2011) Reduction of metastasis using a non-volatile buffer. Clin Exp Metastasis. 28: 841-9. doi: 10.1007/s10585-011-9415-7

[12] Ibrahim-Hashim A, Abrahams D, Enriquez-Navas PM, Luddy K, Gatenby RA, Gillies RJ (2017) Tris-base buffer: a promising new inhibitor for cancer progression and metastasis. Cancer Med. 6: 1720-9. doi: 10.1002/cam4.1032

[13] Ibrahim-Hashim A, Wojtkowiak JW, de Lourdes Coelho Ribeiro M, Estrella V, Bailey KM, Cornnell HH, Gatenby RA, Gillies RJ (2011) Free Base Lysine Increases Survival and Reduces Metastasis in Prostate Cancer Model. J Cancer Sci Ther. Suppl 1.

[14] Robey IF, Baggett BK, Kirkpatrick ND et al. (2009) Bicarbonate increases tumor pH and inhibits spontaneous metastases. Cancer Res. 69: 2260-8. doi: 10.1158/0008-5472.CAN-07-5575

[15] Pilon-Thomas S, Kodumudi KN, El-Kenawi AE et al. (2016) Neutralization of Tumor Acidity Improves Antitumor Responses to Immunotherapy. Cancer Res. 76: 1381-90. doi: 10.1158/0008-5472.CAN-15-1743

[16] Raghunand N, He X, van Sluis R et al. (1999) Enhancement of chemotherapy by manipulation of tumour pH. Br J Cancer. 80: 1005-11. doi: 10.1038/sj.bjc.6690455

[17] Raghunand N, Mahoney B, van Sluis R, Baggett B, Gillies RJ (2001) Acute metabolic alkalosis enhances response of C3H mouse mammary tumors to the weak base mitoxantrone. Neoplasia. 3: 227-35. doi: 10.1038/sj.neo.7900151

[18] Pilot C, Mahipal A, Gillies RJ (2018) Buffer Therapy → Buffer Diet. J Nutr Food Sci. 8. doi: 10.4172/2155-9600.1000685

[19] Hamaguchi R, Narui R, Wada H (2020) Effects of Alkalization Therapy on Chemotherapy Outcomes in Metastatic or Recurrent Pancreatic Cancer. Anticancer Res. 40: 873-80. doi: 10.21873/anticanres.14020

[20] Hamaguchi R, Okamoto T, Sato M, Hasegawa M, Wada H (2017) Effects of an Alkaline Diet on EGFR-TKI Therapy in EGFR Mutation-positive NSCLC. Anticancer Res. 37: 5141-5. doi: 10.21873/anticanres.11934

[21] Abumanhal-Masarweh H, Koren L, Zinger A et al. (2019) Sodium bicarbonate nanoparticles modulate the tumor pH and enhance the cellular uptake of doxorubicin. J Control Release. 296: 1-13. doi: 10.1016/j.jconrel.2019.01.004

[22] Chao M, Wu H, Jin K, Li B, Wu J, Zhang G, Yang G, Hu X (2016) A nonrandomized cohort and a randomized study of local control of large hepatocarcinoma by targeting intratumoral lactic acidosis. Elife. 5. doi: 10.7554/eLife.15691

A direct, enzymatic approach to neutralizing the acidic tumor microenvironment

Although buffer therapies have the potential to neutralize the acidic tumor microenvironment, local administration of buffers is generally not feasible. In order to deliver alkalization therapy to tumors, the Company has developed DOS47, a proprietary technology platform. DOS47 compounds are conjugates of two components: the plant-based urease enzyme and an antibody that binds to a tumor-specific antigen. The antibody component targets the conjugate to tumors and the urease enzyme converts endogenous urea into metabolites that include ammonia and hydroxyl ions, thus raising the pH of the tumor microenvironment.

Product Development

The Company has generated two DOS47 candidates for development: L-DOS47 which is in clinical development and V-DOS47 which is in preclinical research. L-DOS47 is the Company's first targeted therapeutic immune-conjugate developed based on the DOS47 technology.

L-DOS47

L-DOS47 includes an antibody that targets carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6)

Carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6) is a cell surface protein found to be upregulated in several types of cancer, including NSCLC and pancreatic cancer[23]. In lung adenocarcinoma, CEACAM6 expression has been significantly associated with adverse clinical outcome[24]. Similarly, the median survival time of pancreatic adenocarcinoma patients with CEACAM6-positive tumors was significantly shorter than that of patients with CEACAM6-negative disease[25].

L-DOS47 is composed of the jack bean urease enzyme conjugated to approximately 10 copies of a camelid single-chain anti-CEACAM6 antibody[26]. The specificity of L-DOS47 for CEACAM6 was confirmed in *in vitro* binding studies where binding was only observed to cells that express CEACAM6[27]. Immunohistochemistry studies showed binding of L-DOS47 to lung cancer and pancreatic cancer tissues, but not to normal tissues[28]. The ability of L-DOS47 to specifically target tumors was confirmed using a fluorescently-labelled version of L-DOS47. These experiments were performed in a mouse model of lung cancer, and showed that for 12-72 hours after injection, L-DOS47 was localized at the tumor[29].

L-DOS47 has been shown to control tumor growth, reduce metastases, and enhance the effect of chemotherapy in animal models

L-DOS47 was tested in two mouse models: one lung cancer and one pancreatic cancer. In both cases, administration of L-DOS47 reduced tumor growth compared to treatment with a control reagent[30,31,32]. In addition, when lung cancer cells and L-DOS47 were premixed and injected into mice, the presence of L-DOS47 reduced the ability of the tumor cells to colonize the lungs[33]. The ability of L-DOS47 to improve chemotherapy efficacy was observed both in *in vitro* and *in vivo* preclinical experiments. *In vitro* experiments showed that at an acidic pH, L-DOS47 was able to dramatically

---

[23] Blumenthal RD, Leon E, Hansen HJ, Goldenberg DM (2007) Expression patterns of CEACAM5 and CEACAM6 in primary and metastatic cancers. BMC Cancer. 7: 2. doi: 10.1186/1471-2407-7-2

[24] Kobayashi M, Miki Y, Ebina M et al. (2012) Carcinoembryonic antigen-related cell adhesion molecules as surrogate markers for EGFR inhibitor sensitivity in human lung adenocarcinoma. Br J Cancer. 107: 1745-53. doi: 10.1038/bjc.2012.422

[25] Duxbury MS, Matros E, Clancy T et al. (2005) CEACAM6 is a novel biomarker in pancreatic adenocarcinoma and PanIN lesions. Ann Surg. 241: 491-6. doi: 10.1097/01.sla.0000154455.86404.e9

[26] Tian B, Wong WY, Hegmann E, Gaspar K, Kumar P, Chao H (2015) Production and characterization of a camelid single domain antibody-urease enzyme conjugate for the treatment of cancer. Bioconjug Chem. 26: 1144-55. doi: 10.1021/acs.bioconjchem.5b00237

[27] Wong WY (2010) Binding of L-DOS47 to BxPC-3 cells with CEACAM6 gene knockdown. Helix BioPharma Corp. internal report 30BW10708

[28] Wong WY (2010) Immunochemical staining of human tumor tissues by L-DOS47. Helix BioPharma Corp. internal report 30TI10610

[29] Bravo-Grimaldo E (2006) Evaluation of antibody-delivered urease therapy for lung cancer - Phase I. Helix BioPharma Corp. internal report IBD2005-04

[30] Chapdelaine JM (2008) Effect of a test article on the growth of A549 tumor cells in nude mice. Helix BioPharma Corp. internal report 0708MH25.001

[31] Bravo-Grimaldo E (2008) Evaluation of antibody-delivered urease therapy for lung cancer - phase 3. Helix BioPharma Corp. internal report IBD2006.07

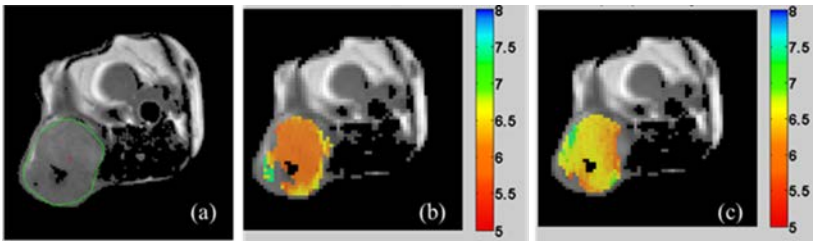
[32] Vasquez RE (2008) Effect of a test article on the growth of A549 tumor cells in nude mice. Helix BioPharma Corp. internal report 0708MH25.002

[33] Vasquez RE (2009) Effect of a test article on A549 tumor cell metastasis in nude mice. Helix BioPharma Corp. internal report 0708MH25.003

increase the cytotoxicity of the weakly basic chemotherapeutic drug doxorubicin[34]. In addition, a preliminary preclinical study showed that pre-treatment with L-DOS47 24 hours before doxorubicin delayed tumor growth in mice bearing a CEACAM6-positive pancreatic tumor[35].

L-DOS47 has been shown to raise the pH of the tumor microenvironment and restore immune-cell activity

Numerous experiments have been performed by the Company which monitored the production of ammonia and increase in pH when L-DOS47 was combined with urea *in vitro.* For examples, see Tian et al and Uger[36]. The ability of L-DOS47 to raise the pH of the tumor microenvironment *in vivo* has been observed in both lung and pancreatic cancer models using multiple imaging methods including ^{31}P-MRS and MRI-CEST[37]. The Company has performed *in vitro* experiments with human $CD8^+$ T cells and has observed that culture at acidic pH increased the expression of the immune-downregulatory molecule programmed cell death protein 1 (PD-1) on the T cells, and that the T cells in acidic conditions reduced their production of the pro-immune cytokine interferon-gamma (IFN-γ)36[7]. L-DOS47 successfully restored the activity of these cells, as observed by reduced expression of PD-1 and increased production of IFN-γ and another pro-immune cytokine, interleukin-2 (IL-2)36. In one preliminary preclinical experiment, treatment with L-DOS47 enhanced the ability of an anti-PD1 antibody to control growth of a pancreatic tumor in a mouse model[38].



CEST MRI of iopamidol for pH imaging [1] of a Panc02 clone 38 SC tumor. (a) T2 weighted image, (b) CEST MRI before L-DOS47 injection, (c) ~30 minutes after 90 µg/ kg L-DOS47 injection. The difference in mean pHs is 0.38 units. L-DOS47 was administered iv. Iopamidol was administered SC, next to the tumor.

In summary, these preclinical experiments demonstrate that L-DOS47 successfully targets CEACAM6-expressing tumors, controls tumor growth, increases the pH of the tumor microenvironment, and is able to improve the efficacy of chemotherapy and immunotherapies. L-DOS47 is currently being tested in clinical trials of both lung and pancreatic cancers. See “Clinical Programs” below.

V-DOS47

V-DOS47 is the second immuno-oncology drug candidate derived from the Company’s DOS47 technology platform. V-DOS47 is an antibody-DOS47 conjugate that targets the vascular endothelial growth factor 2 receptor (VEGFR2). VEGFR2 is overexpressed in breast carcinoma compared with benign breast tissue[39]. In patients with highly estrogen receptor positive (ER^+) forms of breast cancer, the efficacy of tamoxifen treatment negatively correlates with VEGFR2

[34] Uger M (2019) Combined effect of L-DOS47 precursors and doxorubicin in vitro. Helix BioPharma Corp. internal report 30BC10510

[35] Uger M (2019) Effect of adding L-DOS47 to doxorubicin treatment on Panc02/CEACAM6 tumor growth in vivo. Helix BioPharma Corp. internal report 30XM11809

[36] Uger M (2018) *In vitro* effect of lactic acid and L-DOS47 on PD-1 expression, IL-2 production and IFNg production by human primary $CD8^+$ T cells. Helix BioPharma Corp. internal report 30TT11708

[37] Damgaci S, Chao H, Uger MD et al. (2019) Phamacodynamics of targeted urease and checkpoint blockade using CEST and ^{31}P MRSI. Is there a role for hyperpolarized ^{13}C & ^{15}N? World Molecular Imaging Conference, Montreal

[38] Uger M (2019) Effect of L-DOS47 +/- anti-PD-1 antibody on Panc02/CEACAM6 tumor growth *in vivo*. Helix BioPharma Corp. internal report 30XM11805

[39]Kranz A, Mattfeldt T, Waltenberger J (1999) Molecular mediators of tumor angiogenesis: enhanced expression and activation of vascular endothelial growth factor receptor KDR in primary breast cancer. Int J Cancer. 84: 293-8. doi: 10.1002/(sici)1097-0215(19990621)84:3<293::aid-ijc16>3.0.co;2-t

expression[40]. Thus, the Company believe that V-DOS47 may have a therapeutic application in breast cancer. The design and *in vitro* characterization of V-DOS47 has been published[41].

Clinical Programs

The Company has commenced four clinical studies under the L-DOS47 program. Three clinical studies involve the treatment of NSCLC: A Phase I combination study (LDOS001) conducted in the U.S., a Phase I/II monotherapy study concluded in Poland (LDOS002), and a Phase II combination study running in Eastern Europe (LDOS003). A fourth clinical study, a Phase Ib/II study (LDOS006) investigating the treatment of metastatic pancreatic adenocarcinoma, received regulatory approval and is currently being conducted in the U.S. The Company recently applied for a protocol amendment to the LDOS006 clinical trial.

LDOS001 – A Phase I Combination Therapy Trial in Lung Cancer

LDOS001 was a Phase I, open label, dose escalation study of L-DOS47 in combination with standard doublet therapy of pemetrexed/carboplatin in patients with stage IV (TNM M1a and M1b) recurrent or metastatic non-squamous NSCLC. Patients received standard of care doses of pemetrexed [500 mg/m2] and carboplatin [AUC6], respectively, on Day 1 of a 3-week cycle, in combination with L-DOS47 (starting dose 0.59 µg/kg), administered weekly. The objective of the study design was to evaluate safety and tolerability, as well as determine the maximum tolerated dose ("MTD") of L-DOS47, in combination treatment.

Fourteen (14) patients were enrolled across six dosing cohorts, starting at 0.59 and increasing up to 9.0 µg/kg. The MTD was not achieved as none of the patients experienced any dose-limiting toxicity ("DLT"). Fifty percent (50.0%) of patients experienced at least one treatment emergent adverse event assessed as study drug-related, with 14.3% of patients experiencing at least one grade 3/4 drug-related toxicity. Although the study was not designed specifically to assess efficacy, preliminary results showed that of 12 patients evaluable for efficacy, five patients (41.7%) had a partial response ("PR"), four patients (33.3%) experienced stable disease (SD) and three patients (25.0%) had progressive disease ("PD"). The objective response rate was 41.7%, with a median duration of 187 days, and a clinical benefit rate of 75.0% with a median duration of 141 days. Additional reports on L-DOS47 pharmacokinetics and immunogenicity have been completed with the completion of the clinical study report expected to be finalized by December 2021.

L-DOS47, in combination with pemetrexed/carboplatin, was well tolerated with promising anti-tumour activity against non-squamous NSCLC.

LDOS001 Phase I Best Overall Response Summary Efficacy Evaluable(N=12)

	L-DOS47 (All Dosing Cohorts) + Pemetrexed/Carboplatin
Best Overall Response	Overall
Number of Patients[1]	12
Complete Response (CR)	0 (0%)
Partial Response (PR)	5 (41.7%)
Stable Disease (SD)	4 (33.3%)
Progressive Disease (PD)	3 (25.0%)

[1] Number of patients used as denominator to calculate percentages.

LDOS002 – A Phase I/II Monotherapy Trial in Lung Cancer

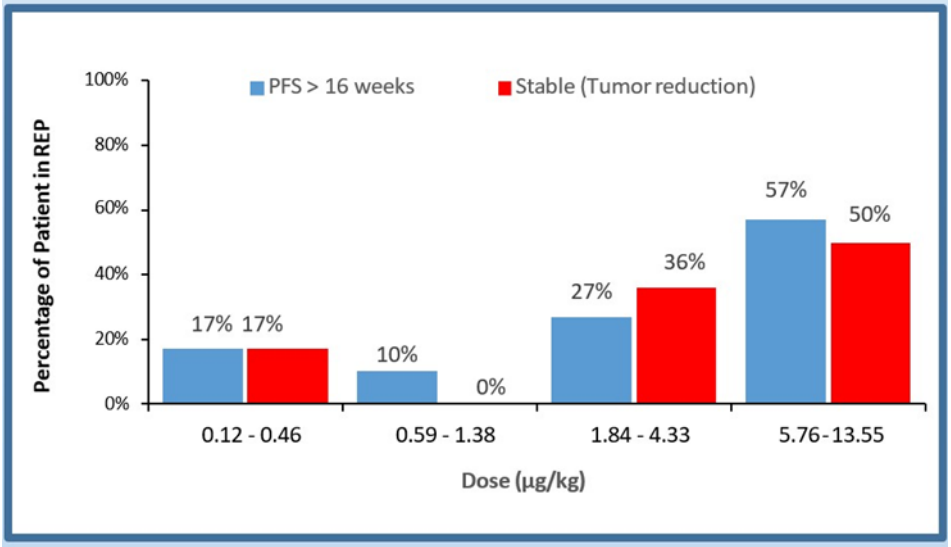
LDOS002 was a Phase I/II open-label, non-randomized, dose escalation study of L-DOS47 as a monotherapy in adult subjects with inoperable, chemo-naïve or refractory Stage IIIb or IV non-squamous NSCLC. The primary objectives of the Phase I portion of the study were to evaluate safety and tolerability of ascending doses of L-DOS47 and define the MTD. Patients received weekly doses of L-DOS47, administered as an intravenous infusion over 14 days, followed by seven days' rest (with one treatment cycle occurring over three weeks).

[40] Rydén L, Stendahl M, Jonsson H, Emdin S, Bengtsson NO, Landberg G (2005) Tumor-specific VEGF-A and VEGFR2 in postmenopausal breast cancer patients with long-term follow-up. Implication of a link between VEGF pathway and tamoxifen response. Breast Cancer Res Treat. 89: 135-43. doi: 10.1007/s10549-004-1655-7

[41] Tian B, Wong WY, Uger MD, Wisniewski P, Chao H (2017) Development and Characterization of a Camelid Single Domain Antibody-Urease Conjugate That Targets Vascular Endothelial Growth Factor Receptor 2. Front Immunol. 8: 956. doi: 10.3389/fimmu.2017.00956

Despite a total of 55 patients being dosed across 16 dose levels ranging from 0.12 up to 13.55 µg/kg, the MTD was not reached. There was only one single DLT of spinal/bone pain reported at the 5.76 µg/kg dose level. The weekly dosing schedule of L-DOS47 for all doses up to 13.55 µg/kg was otherwise well tolerated and most adverse events reported were typical of the population under study. L-DOS47 did not elicit a dose-dependent release of cytokines at doses up to13.55µg/kg. Time of maximum observed plasma drug concentration after dosing ("Tmax") was consistent across dose levels and treatment cycles, occurring within the first hour following the L-DOS47 infusion. There were no safety issues beyond those already observed in pre-clinical toxicology studies or expected in the population of patients being studied.

A dose response trend was observed when comparing the percentage of patients who were progression-free at 16 weeks across dose ranges, according to Response Evaluation Criteria in Solid Tumours ("RECIST") version 1.1. A similar trend was observed when comparing the percentage of patients who had stable disease and had a reduction in target lesions.



L-DOS47 Monotherapy dose response in cohorts

In the Phase II portion of the study, the objective was to make a preliminary assessment of efficacy for L-DOS47 given as monotherapy. Enrolling subjects in the same patient population as in Phase I, patients were dosed at 13.55µg/kg, twice weekly over 14 days, followed by seven days' rest. A total of 21 patients were dosed in the first stage of the Phase II component of the study.

Despite an intensified L-DOS47 monotherapy dosing regimen, evaluation of initial results did not yield ≥1 partial or complete response at any time point as defined by protocol. The Phase II component of the study did not proceed to Phase II, Stage 2 and the development of L-DOS47, as monotherapy treatment of non-squamous, NSCLC was discontinued. Based on the efficacy results of the Phase I/II monotherapy study, Helix is pursuing Phase II studies in combination with therapies that may benefit from the pH-modulating effects of L-DOS47 on solid tumours that express CEACAM6.

LDOS003 – A Phase II Combination Therapy Trial in Lung Cancer

LDOS003 is a Phase II, open-label, randomized study of L-DOS47 in combination with vinorelbine/cisplatin vs vinorelbine/cisplatin alone in patients with lung adenocarcinoma. Vinorebine/cisplatin chemotherapy combination in the U.S. has become infrequent due to the rapidly evolving treatment landscape and the growing prominence of immunotherapies such as Keytruda®. The Company commenced this study based on the use of vinorebine/cisplatin chemotherapy combinations in Eastern European and Asian markets.

The approved protocol called for patients receiving L-DOS47 to be dosed on days 1 and 8 of each 21-day treatment cycle, along with standard vinorelbine/cisplatin chemotherapy for a total of four treatment cycles. The study was divided into two parts. Part I applied a standard 3 + 3 algorithm for dose escalation to determine the L-DOS47 maximum tolerated dose when given in combination with vinorelbine/cisplatin. Cohorts of three patients were recruited into three dosing cohorts (6, 9 and 12 µg/kg). All patients at a given dosing cohort were to complete the first treatment cycle (3-week period) before escalation in subsequent patients were to proceed. The decision for escalation to the next dose level would be made after the safety data had been reviewed by the Trial Steering Committee ("TSC"). If a patient in

any cohort experiences a DLT, an additional three patients would need to be enrolled, for a maximum of up to 18 patients in this initial dose escalation part of the study.

In Part II, after the maximum tolerated dose of L-DOS47 in combination with vinorelbine/cisplatin has been determined, a further 118 patients will be randomized (1:1) to receive L-DOS47 in combination with vinorelbine/cisplatin, or vinorelbine/cisplatin alone. Efficacy will be assessed by time to progression (time from first day of study drug administration to documented disease progression), response rate (proportion of patients with a best overall response of complete response and partial response according to RECIST v. 1.1), and overall survival (time from first day of study drug administration to death due to any cause). Monitoring will include radiological evaluations every second cycle. Safety and tolerability of L-DOS47 in combination will also continue to be evaluated. For all patients, treatment will continue either until the patient experiences disease progression, unacceptable toxicity, the patient withdraws consent or has completed four treatment cycles.

Patient recruitment began in February 2019, but halted in April 2020. At the time, the first two cohorts (6 and 9 µg/kg) in Part I of the study had been completed. Two (2) patients had also been dosed in the third cohort, 12 µg/kg, but the cohort could not be completed due to a shortage in the required vinorelbine dosages from the manufacturer, which was expected to continue into 2021. Consequently, the Company made the decision to terminate further recruitment, proceed to data analysis and not move forward with Part II of the study**.** The clinical report for LDOS003 Phase I LDOS-47 vinorelbine/cisplatin combination study is expected to be complete in March 2022.

LDOS006 – A Phase Ib/II Combination Trial in Pancreatic Cancer

The Company received FDA approval in August 2019 to initiate a new study of L-DOS47 in the treatment of pancreatic cancer. This is an open label, non-randomized study designed to evaluate the safety, tolerability and preliminary anti-tumour activity of L-DOS47 in combination with doxorubicin in patients aged ≥ 18 years old with metastatic pancreatic cancer who have progressed on at least two prior treatment regimens. The trial was initiated in November 2019 and the first patient dosed in December 2019.

The Phase Ib part of the study applies a standard 3 + 3 algorithm for dose escalation to determine the L-DOS47 maximum tolerated dose to use in combination with doxorubicin for the Phase II part of the study. Patients are recruited into three cohorts where each cohort receives increasing weekly dose levels of L-DOS47 in combination with a fixed dose of 20 mg/m2 of doxorubicin weekly, (or 15 mg/m^2 as per the subsequently amended protocol), with four weeks making up one treatment cycle up to a maximum of six cycles. The decision for escalation to the next dose level will be made after all patients in a cohort have completed four weeks of combination treatment and the safety data have been reviewed by the Safety Review Committee of the Company. If a patient in any cohort experiences a dose limiting toxicity, an additional three patients will be enrolled, for a maximum of up to 18 patients in this initial dose escalation part of the study.

The Phase II part of the study will focus on evaluating preliminary anti-tumour activity, as well as continuing to evaluate safety and tolerability of L-DOS47 in combination with doxorubicin. A further 11 additional patients will be enrolled in this phase of the study. Patients will be initiated on the L-DOS47 dose determined in Phase I, in combination with 20 mg/m2 doxorubicin as per the original protocol or 15 mg/m^2 as per the subsequently amended protocol, with tumour marker carbohydrate antigen 19-9 (CA19-9) measurements at each treatment cycle, and radiological assessments every two treatment cycles. Tumour response will be assessed according to RECIST version 1.1. Safety will be assessed by reported adverse events (AEs), serious adverse events (SAEs), physical exams, vital signs, Karnofsky Performance Status, electrocardiogram (ECG), echocardiogram (ECHO)/multi-gated acquisition scan (MUGA), clinical laboratory evaluations (hematology, chemistry, coagulation and urinalysis), and anti-L-DOS47 antibody levels.

Currently a total of fourteen (14) patients have been dosed with L-DOS47 in combination with doxorubicin. Six (6) patients were dosed under the original protocol where patients were initiated on L-DOS47 in combination with 20 mg/m^2 doxorubicin, three (3) of whom withdrew due to disease progression prior to completing the required 4-week cycle in order to be included in the evaluation for dose escalation. Of the remaining three (3) patients, one patient experienced a DLT attributed to doxorubicin and as a result, a protocol amendment adjusting the starting chemotherapy dose was submitted to FDA on December 23, 2020, and patient screening resumed on January 25, 2021. Due to slower enrolment related to challenges resulting from COVID-19 pandemic measures, two additional sites were opened for recruitment in March and April 2021.

Under an amended protocol where patients were initiated on L-DOS47 in combination with 15 mg/m^2 doxorubicin, the first three (3) patients dosed resulted in one patient experiencing a serious adverse event (thromboembolic event). The investigator assessed the event as probably related to L-DOS47, but with alternate causality related to patient's prior medical history of thromboembolic event and advanced pancreatic disease state. The sponsor physician assessed the event as possibly related to doxorubicin chemotherapy, the patient's prior medical history, and an uncontrolled pancreatic cancer state, although a possible relationship to L-DOS47 in combination with doxorubicin could not be ruled out. As this event met the criteria for a DLT, the cohort was expanded and a further 5 patients have since been dosed. Two patients discontinued from the trial prior to completing the required 4-week cycle in order to be included in the

evaluation for dose escalation due to adverse events unrelated to study treatment. Of the remaining three patients, one discontinued due to disease progression, one remains on treatment in the fifth treatment cycle, and one patient continues in the first treatment cycle. This last patient is required to complete the 4-week DLT observation period before safety data for Cohort 1 can be evaluated for dose escalation.

A further revised protocol dated November 9, 2021 was submitted to FDA on November 15, 2021. The main revision is to increase the number of treatment cycles from 6 to 8 cycles, while providing flexibility to administer additional treatment cycles where clinical benefit to patient outweighs risk.

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 studies.

Manufacturing

L-DOS47 is an immunoconjugate drug composed of single chain antibody molecules specific for CEACAM6 that are cross-linked with a purified urease derived from the jack bean plant (Canavalia ensiformis).

The urease component is extracted from jack beans through a multistage process that yields an enzyme with high activity and purity. The llama-derived recombinant antibody is manufactured in E. coli and the purified antibodies are covalently linked to the urease enzyme by a chemical cross-linker into L-DOS47 drug substance. The drug substance is filled and lyophilized into the final L-DOS47 drug product for use in the clinic. The Company has extensively characterized L-DOS47 and maintains a comprehensive analytical program for the drug substance, drug product, and the urease and antibody intermediates.

A 1% Polysorbate 80 diluent is co-mixed with L-DOS47 to prevent protein adsorption to the saline bags and IV tubing that are used to administer the drug to patients in the clinic.

Manufacturing, release, and stability testing of L-DOS47 and the 1% Polysorbate diluent is currently conducted by contract manufacturing organizations ("CMOs") and contract testing laboratories ("CTLs") in Canada and the U.S. The Company requires all CMOs and CTLs to maintain compliance with current GMP and to be licensed by the national regulatory authority in their jurisdiction. Company employees and consultants provide technical, quality, and regulatory oversight for all operations related to L-DOS47 production. Currently, the Company has service and quality agreements with several CMOs/CTLs for clinical-stage manufacturing, testing, and release of the L-DOS47 drug substance and drug product and the 1% Polysorbate diluent.

The Company's supply of L-DOS47 drug product continues to be subjected to stability assays according to ICH Q1A (R2) guidelines. The oldest lot is on extended shelf-life and the last testing point was initially planned for 78M (May 2021) due to a shortage of stability samples. The stability program was subsequently resupplied, and the stability protocol will be extended as long as the product continues to meet specifications. If the product goes Out-of-Specification (OOS) at the real-time storage condition (2-8ºC) for two consecutive pulls before the final time point, further testing may be discontinued.

The CMO that manufactured the L-DOS47 drug substance batch that is currently being used in the clinical studies informed the Company in early 2019 that it would no longer be able to manufacture L-DOS47. In September 2019, the Company signed an agreement with another CMO to reprocess a drug substance batch the Company had kept in reserve. The Company completed the reprocessing of the drug substance batch in June 2020, and after quality control testing and release, the drug substance was transferred to another CMO to complete the fill/finish process. After lyophilization which was completed in early 2021 the drug product lot was placed on a 36M stability program which may be extended if warranted by real-time stability data. If the product goes OOS at the real-time storage condition (2-8ºC) for two consecutive pulls before the final time point, further testing may be discontinued. The new batch recently completed a successful six-month stability test in July 2021 with the next stability test scheduled for completion in December 2021. The Company has another reserve batch of drug substance to produce drug product in the event it needs to do so.

The Company has also been in discussion with another CMO to plan out a technology transfer program to manufacture a new batch of L-DOS47 drug product. As of now, no commitment has been made.

If any of the stability assays for the current batch or new production batch do not meet acceptance criteria, the Company's clinical studies and any planned research and development programs would likely face delays and possibly be cancelled, which could impair the current and future value of the business. See "Risk Factors".

Market and Competition

NSCLC

Based on information published in "Key Statistics for Lung Cancer" by the American Cancer Society (www.cancer.org) in January 2020**,** lung cancer accounts for approximately 25% 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 2020 there will be over 228,820 new lung cancer cases and 135,720 people may die from the disease in the United States. Of these cases, over 80% are anticipated to be of the non-small cell lung cancer (NSCLC) type.

The treatment options for metastatic NSCLC have changed significantly in the last few years due to the clinical success of immunotherapies such as immune checkpoint inhibitors that target Programmed Death 1 ("**PD-1**") or its ligands. However, a significant percentage of patients do not respond to current therapies resulting in an urgent need for additional therapeutic options.

Treatment options for metastatic NSCLC have changed significantly in the last few years due to the clinical success of immunotherapies such as immune checkpoint inhibitors that target PD-1 or its ligands. 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 with Tumours that express PD-L1 whose disease has progressed after treatment.

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 NSCLC. Approval was based on a cohort (G1) of patients enrolled in an open-label, multicenter, multi-cohort study.

Pancreatic Cancer

Pancreatic cancer remains a deadly disease of significant unmet medical needs. In "Key Statistics for Pancreatic Cancer" dated January 2020, the American Cancer Society estimated that in 2020, 57,600 people will be diagnosed with the disease in the US with 47,050 deaths. The most common type of pancreatic cancer is exocrine in nature and approximately 95% of these exocrine cancers are adenocarcinomas.

Treatment options for late-stage metastatic pancreatic cancer patients are limited. Surgery and radiation are used only for symptom relief and chemotherapy remains the primary mode of therapy. Gemcitabine is widely used either alone or in combination with erlotinib (Tarceva), capecitabine, cisplatin or nab-paclitaxel. Other chemo-cocktails are also possible depending on patient tolerability to such cocktails and physician choice of best suitable care. If these lines of therapy are not effective, other combinations such as oxaliplatin and fluoropyrimidine may be used.

Although checkpoint therapy has been shown to be beneficial in certain lung cancers and melanoma, checkpoint therapy clinical studies in pancreatic patients have largely been unsuccessful. While the exact reasons are still to be elucidated, the unique structural and immune environment associated with pancreatic cancer may underlie the lack of success with antibody-based immunotherapies. Technological competition from pharmaceutical companies, biotechnology companies and university researchers is intense and is expected to continue. While the Company is not aware of any other competitors in clinical development of a therapy that targets tumour acidosis, some potential competitors have substantially greater product development capabilities and financial, scientific, marketing and human resources than the Company. See "The Company faces risks in connection with competition and technological change" under the heading "Risk Factors".

INTELLECTUAL PROPERTY

Intellectual Property

The Company protects its intellectual property rights through a robust combination of patent, copyright, trademark and trade secrets as well as with confidentiality and invention assignment agreements.

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.

As of July 31, 2021, the Company had rights to 5 issued U.S. patents, which will expire between July 16, 2023 and January 22, 2036 assuming all required fees are paid, had 6 pending U.S. patent applications, 64 issued foreign

patents, and 42 pending foreign patent applications. The Company's patents and patent applications cover aspects of the Company's current and future product concepts. Some of the pending foreign patent applications preserve an opportunity to pursue patent rights in multiple countries.

As of July 31, 2021, the Company had one registered trademark in Canada.

The Company also relies, in part, upon unpatented trade secrets, know-how and continuing technological innovation, and may in the future rely upon licensing opportunities, to develop and maintain our competitive position. The Company protects its proprietary rights through a variety of methods, including confidentiality and assignment agreements with suppliers, employees, consultants, and others who may have access to the Company's proprietary information.

While there is no active litigation involving any of our patents or other intellectual property rights and we have not received any notices of patent infringement, the Company may be required to enforce or defend its intellectual property rights against third parties in the future.

Patents and other proprietary rights are very valuable to the Company and involve complex legal and factual issues. The Company has no assurance that any or all of its patent applications will result in the issuance of patents. Further, 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. As well, the Company's patents may be invalidated or found enforceable if challenged. Intellectual property laws vary from country to country which may result in varying levels of intellectual property protection.

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 diseases. 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 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 the Company that contain assignment of invention clauses outlining ownership of any intellectual property developed during the course of the individual's relationship with the Company.

Patents

The Company currently owns several patents in respect of the DOS47 technology and has licensed patent rights from the NRC for the antibody component of L-DOS47. In addition to issued patents, the Company has filed several new patent applications around the world.

Cell-Based Therapy

The Company has filed a joint patent application with NRC to protect the use of an antibody for use in cell-based therapies. In addition, the Company filed a new patent application covering the use of anti-VEGFR2 antibodies in cell-based therapy in July 2017.

License Agreements

Xisle Pharma Ventures Trust

In December 2016, the Company 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. Under the terms of the agreement, Xisle paid an up-front fee of USD125,000 and agreed to pay subsequent milestone payments and royalties to the Company as Xisle advances the technology. As part of the agreement, the Company retained marketing rights for Belarus, Bulgaria, the Czech Republic, former Eastern Germany, Hungary, Moldova, Poland, Romania, Russia, Slovakia and Ukraine and non-exclusive rights for co-promotion in Canada. The Company subsequently assigned the foregoing marketing rights which it retained pursuant to an agreement between the Company and HIO, which terminated on June 26, 2020 in connection with the cancellation of intercompany debt owed by HIO to the Company.

NRC

In April 2005, the Company signed a worldwide exclusive license with the NRC through which it obtained the rights to combine a highly specialized camelid-derived single domain antibody with Helix's DOS47 technology to target lung

cancer tissues The Company has certain royalty and milestone payment obligations pursuant to this license agreement. In December 2009, the two parties amended the agreement to better clarify certain definition of terms and the sharing of costs associated with obtaining and maintaining patents.

On February 27, 2017, the Company announced the signing of a licence agreement with the NRC for the worldwide right to anti-CEACAM6 antibody 2A3 for oncology applications. The licence provides Helix the rights to use the antibody in multiple therapeutic modes including cell-based therapy such as CAR-T, new DOS47 conjugates, standalone therapeutic and diagnostic applications on CEACAM6 bearing diseases. The Company has certain royalty and milestone payment obligations pursuant to this license agreement.

ProMab Biotechnologies Inc.

On March 16, 2018, the Company entered into a collaboration agreement with ProMab to co-develop Car-T that target BCMA to treat multiple myeloma. In this collaboration, the Company retains commercial rights for this CAR-T in Canada and Europe. The Company entered into a sublicense agreement for BCMA with HIO whereby the Company will assist in preclinical and early phase clinical planning of the BCMA project. The Company's assistance includes funding a certain portion(s) of the preclinical development stage while HIO leads the regulatory and clinical development of the product in Europe. The Company fulfilled its obligation regarding this collaboration agreement during fiscal 2021. These activities are expected to be coordinated with ProMab who will be developing the product for Asia and the U.S. The Company retains the rights for Canada.

For additional details regarding the foregoing license agreements, see "Material Contracts".

Revenue Generating Activities

The Company has no revenue generating activities.

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. The intention of Company is to enter a structured process that will include preparing the Company to have discussions with potential partners, engaging in dialogue with a targeted group of qualified partners and licensees, and entering negotiations on a prospective partnership, alliance or licensing transaction. 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.

FACILITIES

General office space

The Company's head office is located at 9120 Leslie Street, Suite 205, Richmond Hill, Ontario, Canada. The amended lease arrangement was renewed on July 31, 2020. The lease is a month-to-month lease with a notice period of six months to terminate the lease arrangement.

The Company also leases a small office space in Saskatoon, Saskatchewan on a month-to-month basis with a notice period of 35 days to terminate the lease arrangement.

Laboratories

The Company leases approximately 4,155 sq. ft. in Edmonton, Alberta, Canada under a lease arrangement that originally expired on June 30, 2014. The Company successfully amended the lease terms to expire December 2014 and has since renewed the lease on a month-to-month basis with a notice period of 30 days to terminate the lease arrangement.

EMPLOYEES

The following table depicts the number of full-time equivalent employees in Canada as at July 31:

	2021	2020
Research and development	8.0	8.0
Operating, general and administration	2.0	2.5
	10.0	10.5

None of the Company's employees are covered by collective bargaining agreements.

RISK FACTORS

RISKS AND UNCERTAINTIES

Helix is subject to risks, events and uncertainties, or "risk factors", associated with being a publicly traded company operating in the biotechnology industry, with research and development stage projects in pre-clinical discovery and clinical development and with no expectation of revenue or profits in the foreseeable future and, as such, is heavily dependent on raising sufficient capital on a timely basis in order to advance the Company's drug development programs. 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 actual future 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 AIF, as well as the following:

Risks Related to the Company's Business

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 and/or any convertible debt financing, if secured, would result in dilution to existing shareholders, and that 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 and development 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.

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 drug product candidates. The research and development of drug product candidates require 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 accumulated deficit as at July 31, 2021 is $188,554,000. There can be no assurance that the Company will record earnings in the future or that the drug product candidates under development by us will be approved for sale in Canada, the United States, or elsewhere. Furthermore, there can be no assurance that if such products are approved, they will be successfully commercialized, and the extent of our future losses and the timing of our profitability are highly uncertain. If we are unable to achieve profitability, we may be unable to continue our operations.

The Company faces risks in connection with competition and technological change

The biotechnology industry is 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 has and likely will continue 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. Developments in immunotherapies have resulted in the Company repositioning its L-DOS47 lead drug product candidate away from a front-line monotherapy protocol towards second and third-line combination therapies with existing chemotherapy drugs and possibly in combination with immunotherapies, resulting in additional expenditures and delays in previously anticipated development timelines for L-DOS47. Advancements in technology can impact the Company at any time and as such, any further repositioning, would likely result in additional expenses being incurred by the Company and in further 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 is currently heavily dependent on the success of its lead drug product candidate L-DOS47, which is the only drug candidate currently in clinical development.

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 a nd 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 heavily dependent on the success of a single drug product candidate

The Company's future success is dependent primarily on the regulatory approval and commercialization of a single drug product candidate, L-DOS47, which is the Company's only drug candidate currently in clinical development. The Company does not have any products that have obtained regulatory approval. The Company is conducting early stage research and development initiatives and is currently in the process of developing L-DOS47, which will require further time-consuming and costly research and development. There can be no assurance that L-DOS47 or any other drug product candidate that the Company undertakes to develop will ever be successfully developed or commercialized. As a result, the Company's near-term prospects, including its ability to finance its operations and generate revenue, are substantially dependent on

its ability to obtain regulatory approval for, and, if approved, to successfully commercialize L-DOS47 in a timely manner.

The Company's single lead drug product candidate, L-DOS47, may not be accepted by the market and may never generate revenue and the Company has limited sales, marketing and distribution experience

Even with regulatory approval, the Company may not achieve market acceptance of its lead drug product candidate, L-DOS47, 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 any drug candidate developed by the Company is uncertain. Failure to gain market acceptance of the Company's products or an incorrect estimate in the nature and size of the markets for the Company's products 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 L-DOS47 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.

A failure to obtain necessary financing or a change in the schedule of a clinical trial (which may occur for many reasons, including 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 the commencement or completion of the clinical trial, or result in its suspension or early termination, which could have a material adverse effect on the Company.

We will have significant additional future capital needs in 2021 and beyond and there may be uncertainties as to our ability to raise additional funding in the future to meet these needs

We will require significant additional capital resources to expand our business, in particular the further development of our product candidate, L-DOS47. Advancing our product candidate, marketing for our product, or acquisition and development of any new products or product candidates will require considerable resources and additional access to capital markets. In addition, our future cash requirements may vary materially from those now expected. For example, our future capital requirements may increase if:

- we experience unexpected or increased costs relating to preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, or other lawsuits, brought by either us or our competition;
- we experience scientific progress sooner than expected in our discovery, research and development projects, if we expand the magnitude and scope of these activities, or if we modify our focus as a result of our discoveries;
- we are required to perform additional pre-clinical studies and clinical trials; or
- we elect to develop, acquire or license new technologies, products or businesses.

The Company could potentially seek additional funding through corporate collaborations and licensing arrangements or through public or private equity or debt financing. However, if capital market conditions in general, or with respect to life sciences companies such as ours, are unfavorable, our ability to obtain significant additional funding on acceptable terms, if at all, will be negatively affected. Additional financing that we may pursue may involve the sale of Common Shares which could result in significant dilution to our

shareholders. If sufficient capital is not available, we may be required to delay our research and development projects, which could harm our business, financial condition, prospects or results of operations.

The Company may not obtain adequate protection for its products through its intellectual property

The Company's success depends, in large part, on the Company's ability to protect its competitive position through patents, trade secrets, trademarks, and other intellectual property rights. The Company's success, competitive position and future revenues with respect to its product candidates will depend, in part, on the Company's ability to protect its intellectual property. The Company will be able to protect its proprietary rights from unauthorized use by third parties only to the extent that its proprietary rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. The Company seeks intellectual property protection in various jurisdictions around the world and owns patents and patent applications relating to biological products and technologies in the United States, Canada, Europe and other jurisdictions. The scope and duration of the Company's intellectual property rights vary from country to country depending on the nature and extent of the Company's intellectual property filings, the applicable statutory provisions governing the intellectual property, and the nature and extent of the Company's legal rights. The Company's failure to do so may adversely affect the Company's business and competitive position.

The patent positions of pharmaceutical and biopharmaceutical firms, including the Company's, are uncertain and involve complex questions of law and fact for which certain important legal issues remain unresolved. The patents issued or to be issued to the Company may not provide the Company with any competitive advantage. The Company may not be able to protect its intellectual property rights throughout the world. The Company's patents may be challenged by third parties in patent litigation. In addition, it is possible that third parties with biological products that are very similar to the Company's may circumvent the Company's patents by means of alternate designs or processes. The Company may have to rely on method of use patent protection for its biological products in development and any resulting biological products, which may not confer the same level of protection as protection of the Company's biological products per se. The Company may be required to disclaim part of the term of certain patents in the United States. There may be prior art of which the Company is not aware that may affect the validity or enforceability of a patent claim. There also may be prior art of which the Company is aware, but which the Company does not believe affects the validity or enforceability of a claim, which may, nonetheless ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that the Company's patents would, if challenged, be held by a court to be valid or enforceable or that a competitor's technology or drug would be found by a court to infringe the Company's patents.

Patent terms may be inadequate to protect the Company's competitive position on its product candidates for an adequate amount of time. Patents have a limited lifespan, in most jurisdictions inclusive of the United States, if all maintenance fees are timely paid, the term of protection is a period of 20 years from the filing date of the application. Patent term extensions of up to 5 years may be available in certain countries for patents pertaining to new medicinal ingredients or new combinations of medicinal ingredients for human or veterinary use based upon the delay in regulatory review. Even if patents covering the Company's product candidates are obtained, once the patent life and any patent term extension have expired, the Company may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, the Company's owned and licensed patent portfolio may not provide the Company with sufficient rights to exclude others from commercializing products similar or identical to the Company's.

Patent applications relating to or affecting the Company's business may have been filed by a number of pharmaceutical and biopharmaceutical companies and academic institutions. The technologies in these applications or patents may cover the Company's technologies, and such conflict could create freedom to operate issues. The Company's granted patents could be challenged, invalidated or found unenforceable in interference and derivation proceedings, and post grant proceedings including re-examination, *Inter Parte* Review and Post-Grant Review, in the United States. The Company's granted patents could also be challenged and revoked in opposition proceedings in certain countries outside of the United States such as in Europe. In addition to patents, the Company relies on trade secrets and proprietary know-how to protect its intellectual property. The Company generally requires employees, consultants, outside scientific collaborators, and sponsored researchers and other advisors to enter into confidentiality agreements. These agreements provide that all confidential information developed or made known to the individual during the course of the individual's relationship with the Company is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all of the technology that is conceived by the individual during the course of employment is the Company's exclusive property. These agreements may not provide meaningful protection or adequate remedies in the event of unauthorized use or disclosure of proprietary information. In addition, it is possible that third parties could independently develop proprietary information and techniques substantially similar to the Company's or otherwise gain access to the Company's trade secrets.

The Company may obtain the right to use certain technology under license agreements with third parties. The Company's failure to comply with the requirements of material license agreements could result in the termination of such agreements, which could cause the Company to terminate the related development program and cause a complete loss of investment in that program. As a result of the foregoing factors, the Company may not be able to rely on its intellectual property to protect the Company's products in the marketplace.

Patent litigation is costly and time consuming and may subject the Company to liabilities

The Company's involvement in any patent litigation, opposition, or other administrative proceedings will likely cause the Company to incur substantial expenses, and the efforts of technical and management personnel will be significantly diverted. In addition, the Company may not have the financial means defend its patents and in the event it does, an adverse determination in litigation could subject the Company to significant liabilities, including, but not limited to, monetary damages.

Security breaches and other disruptions could compromise the Company's information and expose the Company to liability, which would cause the Company's business and reputation to suffer

In the ordinary course of our business, the Company collects and stores sensitive data, including intellectual property, proprietary business information and that of our suppliers and business partners, and personally identifiable information of our collaborators and employees, on our networks and on shared cloud services. The secure processing, maintenance and transmission of this information is critical to our operations. Despite our security measures, our information technology and infrastructure may be exposed to malware, cyberattacks, attacks by hackers or breached due to employee error, malfeasance, or other disruptions. Any such breach could compromise our networks and the information stored there could be accessed, publicly disclosed, lost or stolen. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, disrupt our operations and damage our reputation, which could adversely affect our business and competitive position.

Further, some of our partners may store personal or confidential information that we share with them. If these third parties fail to implement adequate data-security practices or fail to comply with our terms and policies, sensitive data may be improperly accessed, acquired, or disclosed. And even if these third parties take all these steps, their networks and information technology systems may still suffer a security breach, which could compromise our data.

The Company may infringe the intellectual property rights of others

The Company's commercial success depends significantly on the Company's ability to operate without infringing on the patents and other intellectual property rights of third parties. There could be issued patents of which the Company is not initially aware that the Company's products infringe or patents that the Company believes it does not infringe, but that the Company may ultimately be found to infringe. Patent applications are maintained in secrecy from the time of filing until publication. The publication of discoveries in the scientific or patent literature frequently occurs later than the date on which the underlying discoveries were made and patent applications were filed. There may be currently pending patent applications of which the Company is unaware that may later result in issued patents that the Company's products infringe.

The biopharmaceutical industry has produced a proliferation of patents in jurisdictions around the world. The coverage of patents is subject to interpretation by the courts of a particular jurisdiction, and the interpretation is not always uniform. The Company believes that the sale or use of its primary biological product candidate, L-DOS47 would not infringe any valid claim of patents, although there can be no assurances of this. In the event of an infringement or violation of another party's patent, the Company may not be able to enter into licensing arrangements or make other arrangements at a reasonable cost. Any inability to secure licenses or alternative technology could result in delays in the introduction of drugs or lead to prohibition of the manufacture or sale of drugs by the Company.

Third parties may initiate legal proceedings alleging that the Company is infringing their intellectual property rights, the outcome of which would be uncertain and could harm the Company's business

Third parties may assert patent or other intellectual property infringement claims against the Company or its other licensors arising from the manufacture, use, or sale of the Company's current or future product candidates. An unfavorable outcome could result in loss of patent rights and require the Company to cease using the related technology or to attempt to license rights to it from the prevailing party. The Company's business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. The Company may not have the financial means and wherewithal to defend against third party claims and in

the event it does, defense of litigation proceedings may fail and, even if successful, may result in substantial costs and distract the Company's management and other employees. In the event of a successful claim of infringement against the Company, the Company may have to pay substantial damages, including treble damages and legal fees for willful infringement, pay royalties, redesign its infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

The Company may become involved in lawsuits or other proceedings to protect or enforce the Company's patents or other intellectual property, which could be expensive, time consuming and unsuccessful

Competitors may infringe the Company's patents or other intellectual property. The Company may not have the financial means and wherewithal to defend its patents or other intellectual properties and in the event the Company was to initiate legal proceedings against a third party to enforce a patent covering the Company's product candidates, the defendant could counterclaim that the patent covering the Company's product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, enablement, or clarity. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the United States Patent and Trademark Office, or "USPTO", or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. The validity of the Company's current or future patents or patent applications or those of the Company's licensors may also be challenged in interference or derivation proceedings, opposition, post grant review, inter partes review, or other similar enforcement and revocation proceedings, provoked by third parties or brought by the Company. The Company's patents could be found invalid, unenforceable, or their scope significantly reduced.

The Company may be subject to claims challenging the inventorship of the Company's patents and other intellectual property

The Company or its licensors may be subject to claims that former employees, collaborators or other third parties have an interest in the Company's owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, the Company or its licensors may have inventorship disputes arise from conflicting obligations of employees, collaborators, consultants or others who are involved in developing the Company's product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship of the Company's or its licensors' ownership of the Company's owned or in-licensed patents, trade secrets or other intellectual property. The Company may not have the financial means to defend such claims and in the event the Company or its licensors fail in defending any such claims, in addition to paying monetary damages, the Company may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to the Company's product candidates. Even if the Company is successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on the Company's business, financial condition, results of operations and prospects.

The Company may be subject to claims that its employees, collaborators, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that the Company's employees have wrongfully used or disclosed alleged trade secrets of their former employers

As is common in the biotechnology and pharmaceutical industry, the Company employs individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including the Company's competitors or potential competitors. Although the Company tries to ensure that its employees, collaborators, consultants and independent contractors do not use the proprietary information or know-how of others in their work for the Company, the Company may be subject to claims that the Company or its employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of the Company's employees' former employers or other third parties. Litigation may be necessary to defend against these claims. The Company may not have the financial means to defend such claims and in the event the Company fails in defending any such claims, in addition to paying monetary damages, the Company may lose valuable intellectual property rights or personnel, which could adversely impact the Company's business. Even if the

Company is successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and the Company's patent protection could be reduced or eliminated for non-compliance with these requirements

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. The Company has systems in place to remind the Company to pay these fees, and the Company employs an outside firm and relies on its outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. The Company employs reputable law firms and other professionals to help the Company comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, the Company's competitors might be able to enter the market and this circumstance would have a material adverse effect on 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.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming, expensive and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. It is not uncommon for companies in the biopharmaceutical industry to suffer significant setbacks in advanced clinical trials due to nonclinical findings made while clinical studies were underway and safety or efficacy observations made in clinical studies, including previously unreported adverse events. Our future clinical trial results may not be successful, and notwithstanding any potential promising results in earlier studies, we cannot be certain that we will not face similar setbacks. The historical failure rate for product candidates in our industry is high. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an New Drug Application, or NDA, or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

We may not have the necessary capabilities, including adequate staffing, to successfully manage the execution and completion of any future clinical trials we initiate in a way that leads to our obtaining marketing approval for our product candidates in a timely manner, or at all. This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, results of operations and prospects.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate or may restrict its distribution. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

We have not previously submitted an NDA to the FDA or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approvals to market one or more of our product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patients that we are targeting for our product candidates are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

We plan to seek regulatory approval to commercialize our product candidates both in the United States and the European Union and in additional foreign countries. While the scope of regulatory approval is similar in other countries, to obtain separate regulatory approval in many other countries we must comply with numerous

and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. The clinical evaluation of our product candidates in patients is still in the early stages and it is possible that there may be side effects associated with their use. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, we, the FDA, the IRBs at the institutions in which our studies are conducted, or the DSMB could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such products;
- we may be required to recall a product or change the way such a product is administered to patients;
- additional restrictions may be imposed on the marketing or distribution of the particular product or the manufacturing processes for the product or any component thereof;
- regulatory authorities may require additional warnings on the label, such as a “black box” warning or contraindication;
- we may be required to implement Risk Evaluation and Mitigation Strategies, or REMS, or create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- our product may become less competitive; and
- our reputation may Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate or for particular indications of a product candidate, if approved, and could significantly harm our business, results of operations and prospects.

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 be unable 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 Company relies significantly on licensed intellectual property. If the Company were to lose its rights to licensed intellectual property, the Company would not be able to continue developing or commercializing L-DOS47. If the Company breaches the agreement with NRC under which it licenses the use, development and commercialization rights to a lung cancer antibody in order to develop and commercialize L-DOS47 or any other future product candidate or technology from third parties or if certain insolvency events were to occur, the Company could lose license rights that are critical to its business

The Company has an exclusive worldwide license to a lung cancer antibody necessary to develop and commercialize L-DOS47 pursuant to a license agreement with NRC that is critical to the Company's business, which is subject to termination for breach of certain terms and, therefore, the Company's rights may only be available for as long as the Company's development and commercialization activities are sufficient to meet the terms of the license. In addition, the Company may need to enter into additional license agreements in the future. The Company's existing license agreements impose, and any future license agreements may impose on the Company, various developments, regulatory and/or commercial diligence obligations, payment of milestones and/or royalties and other obligations. If the Company fails to comply with its obligations under these agreements, or the Company is subject to a bankruptcy, the licensor may have the right to terminate the license, in which event the Company would not be able to market products covered by the license, which would have a material adverse effect on the Company's business, financial condition, results of operations and prospects. Moreover, the Company's current or future licenses may provide for a reversion to the licensor

of the Company's rights in regulatory filings or other intellectual property or data that the Company regards as its own in the event the license terminates under certain circumstances, such as due to breach.

Licensing of intellectual property is of critical importance to the Company's business and involves complex legal, business and scientific issues. Disputes may arise between us and the Company's licensors regarding intellectual property subject to a license agreement, including with respect to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the rights of the Company's licensors under the license agreements; and
- the Company's diligence obligations with respect to the use of the licensed technology in relation to the Company's development and commercialization of L-DOS47 and any future product candidates, and what activities satisfy those diligence obligations.

Any disputes with the Company's licensors over intellectual property that the Company has licensed from them may prevent or impair the Company's ability to maintain its current licensing arrangements on acceptable terms. Termination or expiry of the Company's license agreements could result in the loss of significant rights and could materially harm the Company's ability to further develop and commercialize L-DOS47 or other future product candidates.

In addition, the agreements under which the Company currently licenses intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what the Company believes to be the scope of its rights to the relevant intellectual property or technology, or increase what the Company believes to be its financial or other obligations under the relevant agreement, either of which could have a material adverse effect on the Company's business, financial condition, results of operations, and prospects. Moreover, if disputes over intellectual property that the Company has licensed prevent or impair the Company's ability to maintain its current licensing arrangements on commercially acceptable terms, the Company may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on the Company's business, financial conditions, results from operations and prospects.

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.

We are substantially dependent on third parties for the manufacture of our clinical supplies of our product candidates, and we intend to rely on third parties to produce commercial supplies of any approved product candidate. Therefore, our development of our products could be stopped or delayed, and our commercialization of any future product could be stopped or delayed or made less profitable if third party manufacturers fail to obtain approval of the FDA or comparable regulatory authorities or fail to provide us with drug product in sufficient quantities or at acceptable prices

The manufacture of biotechnology and pharmaceutical products is complex and requires significant expertise, capital investment, process controls and know-how. Common difficulties in biotechnology and pharmaceutical manufacturing may include: sourcing and producing raw materials, transferring technology from chemistry and development activities to production activities, validating initial production designs, scaling manufacturing techniques, improving costs and yields, establishing and maintaining quality controls and stability requirements, batch lot expiries, eliminating contaminations and operator errors, and maintaining compliance with regulatory requirements. We do not currently have nor do we plan to acquire the infrastructure or capability internally in accordance with cGMP prescribed by the FDA or to produce an adequate supply of compounds to meet future requirements for clinical trials and commercialization of our products. Drug manufacturing facilities are subject to inspection before the FDA will issue an approval to market a new drug product, and all of the manufacturers that we intend to use must adhere to the cGMP regulations prescribed by the FDA.

We expect therefore to rely on third-party manufacturers for clinical supplies of our product candidates that we may develop. These third-party manufacturers will be required to comply with current good manufacturing practices, or GMPs, and other applicable laws and regulations. We will have no control over the ability of these third parties to comply with these requirements, or to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authorities do not approve the facilities of these third parties for the manufacture of our other product candidates or any products that we may successfully develop, or if it withdraws any such approval, or if our suppliers or contract manufacturers decide they no longer want to supply or manufacture for us, we may need to find alternative manufacturing facilities, in which case we might not be able to identify manufacturers for clinical or commercial supply on acceptable terms, or at all. Any of these factors would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates and adversely affect our business.

We and/or our third-party manufacturers may be adversely affected by developments outside of our control, and these developments may delay or prevent further manufacturing of our products. Adverse developments may include labor disputes, resource constraints, shipment delays, inventory shortages, lot failures, unexpected sources of contamination, lawsuits related to our manufacturing techniques, equipment used during manufacturing, or composition of matter, unstable political environments, acts of terrorism, war, natural disasters, and other natural and man-made disasters. If we or our third-party manufacturers were to encounter any of the above difficulties, or otherwise fail to comply with contractual obligations, our ability to provide any product for clinical trial or commercial purposes would be jeopardized. This may increase the costs associated with completing our clinical trials and commercial production. Further, production disruptions may cause us to terminate ongoing clinical trials and/or commence new clinical trials at additional expense. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications or pass safety inspections. If production difficulties cannot be solved with acceptable costs, expenses, and timeframes, we may be forced to abandon our clinical development and commercialization plans, which could have a material adverse effect on our business, prospects, financial condition, and the value of our securities.

We, or third-party manufacturers on whom we rely, may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any

In order to conduct clinical trials of our product candidates and commercialize any approved product candidates, we, or our manufacturers, will need to manufacture them in large quantities. We, or our manufacturers, may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If we, or any of our manufacturers, are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing, and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. If we are unable to obtain or maintain third-party manufacturing for commercial supply of our product candidates, or to do so on

commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully.

Our failure to find third party collaborators to assist or share in the costs of product development could materially harm our business, financial condition and results of operations

Our strategy for the development and commercialization of our proprietary product candidates may include the formation of collaborative arrangements with third parties. Existing and future collaborators have significant discretion in determining the efforts and resources they apply and may not perform their obligations as expected. Potential third party collaborators include biopharmaceutical, pharmaceutical and biotechnology companies, academic institutions and other entities. Third-party collaborators may assist us in:

- funding research, preclinical development, clinical trials and manufacturing;
- seeking and obtaining regulatory approvals; and
- successfully commercializing any future product candidates.

If we are not able to establish further collaboration agreements, we may be required to undertake product development and commercialization at our own expense. Such an undertaking may limit the number of product candidates that we will be able to develop, significantly increase our capital requirements and place additional strain on our internal resources. Our failure to enter into additional collaborations could materially harm our business, financial condition and results of operations.

In addition, our dependence on licensing, collaboration and other agreements with third parties may subject us to a number of risks. These agreements may not be on terms that prove favorable to us and may require us to relinquish certain rights in our product candidates. To the extent we agree to work exclusively with one collaborator in a given area, our opportunities to collaborate with other entities could be curtailed. Lengthy negotiations with potential new collaborators may lead to delays in the research, development or commercialization of product candidates. The decision by our collaborators to pursue alternative technologies or the failure of our collaborators to develop or commercialize successfully any product candidate to which they have obtained rights from us could materially harm our business, financial condition and results of operations.

We rely on third parties to conduct our preclinical and clinical trials. If these third parties do not successfully perform their contractual legal and regulatory duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed

We have relied upon and plan to continue to rely upon third-party medical institutions, clinical investigators, contract laboratories and other third party CROs to monitor and manage data for our ongoing preclinical and clinical programs. We rely on these parties for execution of our preclinical and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with cGCPs, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area, or EEA, and comparable foreign regulatory authorities for all of our products in clinical development.

Regulatory authorities enforce these cGCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with cGCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices, or cGMP, regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our on-going clinical, nonclinical and preclinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval

for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If the third parties conducting our GLP preclinical studies or our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to their failure to adhere to our clinical trial protocols or to GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

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 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 four 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 its current resident Canadian

director in the future and is unable to find a resident Canadian director to fill the resulting vacancy, the Board will be prevented from taking any action other than appointing an additional resident Canadian director until such time as a new resident Canadian director has been appointed such that at least 25% of the Company's directors are resident Canadians.

The Company employs a small number of employees who have many years of technical knowledge of the Company's technology and two senior officers, the CEO and CFO. COVID-19 imposes a high risk to all of the Company's activities. The Company has established a policy to diligently monitor developments. Because the situation is fluid, the Company will be updating its staff whenever necessary. The Company has implemented and communicated a policy to all staff in order mitigate any potential risk.

In addition, the Company does not carry key-person 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 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. Fluctuations in the value of foreign currencies relative to the Canadian dollar could cause us to incur currency exchange losses.

The Company may incur losses due to adverse decisions by tax authorities or changes in law

The Company's income tax reporting is subject to audit by tax authorities. The effective tax rate may change from year to year based on the mix of income; non-deductible expenses; changes in tax law; and changes in the estimated values of future income tax assets and liabilities.

The Company may enter into transactions and arrangements in the ordinary course of business in which the tax treatment is not entirely certain. The Company must therefore make estimates and judgments in determining its consolidated tax provision. The final outcome of any audits by taxation authorities may differ from estimates and assumptions used in determining the consolidated tax provisions and accruals. This could result in a material effect on the Company's scientific research and experimental development tax credits, income tax provision, financial position and the net income/loss for the period in which such determinations are made.

The Company is subject to taxation in Canada. The Company's effective tax rate and tax liability are determined by a number of factors, including the amount of taxable income, the tax rates, The application of these tax laws and related regulations is subject to legal and factual interpretation, judgment and uncertainty. An adverse interpretation or ruling by a taxing authority in a jurisdiction in which the Company operates or a

change in law could increase the Company's tax liability or result in the imposition of penalty payments, which could adversely impact the Company's operating results.

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

The Company's Common Shares are publicly traded on the TSX. As a public company, the Company is subject to the reporting requirements of Canadian securities regulators, the listing requirements of any stock exchange on which its Common Shares are listed for trading 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.

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 the Company's consolidated financial statements or cause us to fail to meet the Company's reporting obligations or fail to prevent fraud; and in that case, the Company's shareholders could lose confidence in the Company's financial reporting, which would harm the Company's business, could negatively impact the price of the 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 the Company's financial reporting, which would harm the Company's business, negatively impact the price of the Common Shares and also prevent the Company from raising additional capital. Even if the Company were to conclude that its 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 the Company's business**,** negatively impact the trading price of the Common Shares and prevent the Company from raising additional capital.

Our results of operations may be negatively impacted by the COVID-19 outbreak

The Company's business, operations and financial condition could be materially and adversely affected by the outbreak of epidemics or pandemics or other health crises, including the COVID-19 pandemic. As a result of the COVID-19 outbreak, the Company may experience disruptions that could severely impact its business, preclinical studies and clinical trials, including:

- delays or difficulties in enrolling patients in our clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal, provincial or state governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- interruption or delays in the operations of the FDA, which may impact approval timelines;
- interruption of, or delays in receiving supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems; and
- limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people.

In addition, the trading prices for the Common Shares and the securities of other biopharmaceutical companies have been highly volatile as a result of the COVID-19 epidemic. As a result, the Company may face difficulties raising capital through sales of our securities, and such sales may be on unfavorable terms, if at all. The COVID-19 outbreak continues to rapidly evolve. The extent to which the outbreak may impact our business, preclinical studies and clinical trials will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the disease, the duration of the outbreak, travel restrictions and other measures implemented in Canada, the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the Canada, the United States and other countries to contain the disease.

The spread of COVID-19 has resulted in a sharp decline in global economic growth as well as causing increased volatility and declines in financial markets. If the COVID-19 pandemic is prolonged, or further diseases emerge that give rise to similar effects, the adverse impact on the global economy could deepen and result in further declines in global economic growth and financial markets. Accordingly, the full impact of the COVID-19 pandemic on the global economy and financial markets is uncertain and may have an adverse effect on the Company.

To the extent the COVID-19 pandemic adversely affects our business and financial results, it may also have the effect of heightening many of the other risks described in this AIF. Because of the highly uncertain and dynamic nature of events relating to the COVID-19 pandemic, it is not currently possible to estimate the impact of COVID-19 on the Company. However, these effects could have a material impact on our business, operations and financial condition.

Risks Related to the Common Shares

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

The market 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 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 but not limited to, the following:

- actual or anticipated fluctuations in the Company's quarterly results of operations;
- recommendations by securities research analysts;

- changes in the economic performance or market valuations of companies in the industry in which the Company operates;
- addition or departure of the Company's executive officers and other key personnel;
- release or expiration of transfer restrictions on outstanding Common Shares;
- sales or perceived sales of additional Common Shares;
- operating and financial performance that vary from the expectations of management, securities analysts and investors;
- regulatory changes affecting the Company's industry generally and its business and operations;
- announcements of developments and other material events by the Company or its competitors;
- fluctuations to the costs of vital production materials and services;
- changes in global financial markets and global economies and general market conditions, such as interest rates and pharmaceutical product price volatility;
- significant acquisitions or business combinations, strategic partnerships, joint ventures or capital commitments by or involving the Company or its competitors;
- operating and share price performance of other companies that investors deem comparable to the Company or from a lack of market comparable companies;
- news reports relating to trends, concerns, technological or competitive developments, regulatory changes and other related issues in the Company's industry or target markets; and the outbreak of epidemics, pandemics or other health crises including COVID-19.

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 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.

Shareholders of the Company may face dilution from future equity or convertible debt financings or through the exercise of stock options, warrants or other securities convertible or exchangeable into Common Shares

To attract and retain key personnel, the Company has granted options to its key employees, directors and consultants to purchase Common Shares 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 the exercise of a significant number of such options and/or warrants may result in significant dilution to 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 securities and warrants may also result in significant dilution to the shareholders of the Company.

The Company cannot predict the size or nature of future sales or issuances of securities or the effect, if any, that such future sales and issuances will have on the market price of the Common Shares. Sales or issuances of substantial numbers of Common Shares or other securities that are convertible or exchangeable into Common Shares, or the perception that such sales or issuances could occur, may adversely affect prevailing market prices of the Common Shares. With any additional sale or issuance of Common Shares or other securities that are convertible or exchangeable into Common Shares, investors will suffer dilution to their voting power and economic interest in the Company. Furthermore, to the extent holders of the Company's stock options or other convertible securities convert or exercise their securities and sell the Common Shares

they receive, the trading price of the Common Shares may decrease due to the additional amount of Common Shares available in the market.

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 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.

The Company does not expect to pay any cash dividends for the foreseeable future

Investors should not rely on an investment in the Common Shares to provide dividend income. The Company does not anticipate that it will pay any cash dividends to holders of the Common Shares in the foreseeable future. Instead, the Company plans to retain any earnings to maintain and expand its operations. In addition, any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on the Common Shares. Accordingly, investors must rely on sales of their Common Shares after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase Common Shares.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research about the Company's business, the share price and trading volume of the Common Shares could decline

The trading market for the Common Shares will depend, in part, on the research and reports that securities or industry analysts publish about the Company or its business. If one or more of the analysts who cover the Company downgrade the Common Shares or publish inaccurate or unfavorable research about the Company's business, the Company's share price would likely decline. In addition, if the Company's operating results fail to meet the forecast of analysts, the Company's share price would likely decline. If one or more of these analysts cease coverage of the Company or fail to publish reports on the Company regularly, demand for the Common Shares could decrease, which might cause the share price and trading volume of the Common Shares to decline.

DIVIDEND POLICY

To date, the Company has not paid any dividends on the outstanding Common Shares and has no current intention to declare dividends on its Common Shares in the foreseeable future. Any decision to pay dividends on the Common Shares in the future will be dependent upon the financial requirements of the Company to finance future growth, the financial condition of the Company and other factors that the Board may consider appropriate in the circumstances. The Company has no restrictions on the payment of dividends other than those provided under the provisions of the *Canada Business Corporations Act* (the "CBCA") and the policies of the TSX.

CAPITAL STRUCTURE

Share capitalization

The Company's articles authorize the issuance of an unlimited number of Common Shares and 10,000,000 preferred shares issuable in series. As at July 31, 2021, the Company had 141,133,017 Common Shares and nil preferred shares issued and outstanding.

Common Shares

The holders of the Common Shares are entitled to receive notice of and to attend all meetings of the shareholders of the Company and have one vote for each Common Share held at all meetings of shareholders.

Subject to the rights, privileges, restrictions and conditions attaching to any other class or series of shares of the Company, the holders of Common Shares are entitled to receive dividends as and when declared by the Board, in such amount and in such form as the Board may from time to time determine, and subject to the limitations on declaration of dividends prescribed in the CBCA. All dividends which the Board may declare on the Common Shares must be declared and paid in equal amounts per share on all Common Shares at the time outstanding.

In the event of the dissolution, liquidation or winding-up of the Company, whether voluntary or involuntary, or in the event of any other distribution of the Company's assets among its shareholders for the purpose of winding-up its affairs, the holders of the Common Shares shall, subject to the rights of the holders of any other class of shares of the Company, be entitled to receive such assets of the Company upon such distribution.

Preferred shares

The preferred shares of the Company may at any time or from time to time be issued in one or more series. The directors may alter by resolution the articles of the Company, to fix or change the number of shares in, and to determine the designation, rights, privileges, restrictions and conditions attaching to the shares of each series of preferred shares. The directors may also confer on the holders of any series of preferred shares the right to notice of or to be present or to vote, at any general meeting of the shareholders of the Company. Preferred shares shall be entitled to preference over the Common Shares and any other shares of the Company ranking junior to the preferred shares in the event of any liquidation, dissolution or winding-up of the Company or any distribution of its assets for the purpose of winding-up its affairs, whether voluntary or involuntary. The preferred shares of each series will rank in parity with the preferred shares of every other series with respect to priority in the payment of dividends and in the distribution of assets in the event of liquidation, dissolution or winding-up of the Company.

Warrants

Warrants have been issued by the Company in connection with the sale of units of the Company, with each unit consisting of one Common Share and one Warrant. The Warrants of the Company are subject to certain restrictions on transfer as set out in the applicable certificates representing such Warrants. The certificates provide that any rights under such certificates, including any beneficial interest therein, are not transferrable or assignable to any other person by the holder of such certificate without the prior written consent of the Company.

As of July 31, 2021, there were Warrants outstanding to purchase an aggregate of 69,377,969 Common Shares at exercise prices ranging from $0.70 per share to $2.24 per share (subject to adjustment in the event of a subdivision, consolidation or reclassification of the Common Shares prior to the expiry time for such Warrant). The Warrants expire at various times between December 28, 2021 and December 29, 2025.

Convertible Security

On May 12, 2021, the Company issued the $4,112,500 face value Convertible Security to Lind pursuant to the closing of the First Tranche. See “Material Contracts” for additional information relating to the Convertible Security issued under the First Tranche and the Convertible Security issuable under any second tranche of the Lind Agreement.

MARKET FOR SECURITIES

Trading Price and Volume

The Common Shares began trading on the TSX on June 3, 1996. The current stock symbol is “HBP”. The following table sets forth the price ranges and trading volumes of the Common Shares on the TSX for the respective periods.

2020	High	Low	Volume
August	$0.58	$0.50	107,772
September	$0.50	$0.35	224,287
October	$0.41	$0.30	728,610
November	$0.35	$0.29	454,821
December	$0.42	$0.25	2,879,308

2021	High	Low	Volume
January	$1.05	$0.42	1,167,372
February	$1.16	$0.75	1,305,429
March	$0.93	$0.77	643,584
April	$0.95	$0.83	556,573
May	$0.96	$0.88	408,312
June	$0.97	$0.81	265,386
July	$0.95	$0.61	186,274
August	$0.92	$0.68	158,025
September	$0.85	$0.55	133,865
October	$0.60	$0.40	537,153
November	$0.62	$0.45	336,024
December 1 to 8	$0.51	$0.44	36,750

The Common Shares are quoted on the Frankfurt, Stuttgart, Munich and Berlin Stock Exchanges, under the trading symbol “HBP” though trading is negligible.

DIRECTORS AND OFFICERS

Name, Occupation and Securities Holding

The directors of the Company are elected at each annual general meeting of the Company and hold office until the next annual general meeting or until their successors are elected.

The directors have appointed an Audit Committee consisting of three directors, namely, Artur Gabor (Chair), Krzysztof Saczek and Ireneusz Fąfara. Mr. Saczek was appointed to the Audit Committee subsequent to the year ended July 31, 2021 in connection with the appointment of Slawomir Majewski as the Company's Interim CEO, which required Mr. Majewski to step down from the Audit Committee in order for the Company to comply with its Audit Committee independence requirements under applicable securities laws.

During the year ended July 31, 2021, the directors appointed a NASDAQ listing committee to assess the possibility of a listing of Common Shares on NASDAQ or another U.S. stock exchange, which committee consists of the same three directors as the Audit Committee, namely, Artur Gabor (Chair), Slawomir Majewski and Ireneusz Fąfara.

The following is a list of directors and executive officers of the Company, as of the date of this Annual Information Form, along with a brief biography:

- Sławomir Majewski
  Director since October 2012 (independent director)
  Interim Chief Executive Officer (since September 2021)
  Residence: Warsaw, Poland
  Age: 65

  Prof. Majewski has been the Head of the Department of Dermatology and Venereology, Center of Diagnostics and Treatment of STD, Warsaw Medical University, Poland, since 1998, Deputy Rector for Science and International Relations at the Medical University of Warsaw in 20082016, Coordinator of the Polish Center of Preclinical Studies and Technology in 2008-2016 and a member of the scientific advisory board at the Polish Ministry of Health. Prof. Majewski is /was also a member of several national and international societies and scientific institutions including the Polish Academy of Sciences, European Society of Dermatological Research, European Academy of Dermatology and Venereology, European Association for Cancer Research, American Association for Cancer Research, International Advisory Committee of the Archives of Dermatology and the International Editorial Committee of the Journal of American Academy of Dermatology. He was also member of the board of the European Society for Dermatological Research from 2000 to 2004 and from 2003 to 2008, Prof. Majewski was a member of the International Steering Committee of the FUTURE II Study on the quadrivalent HPV vaccine. He is also a former member of the Board, having served from 2008 to 2009. Prof. Majewski was appointed to Helix Immuno-Oncology S.A.'s (presently 4CellTherapies) Supervisory Board on September 1, 2017 and on January 31, 2018 became Chair of the Supervisory Board. Since September 2021 he is Interim CEO of the Company.

- Ireneusz Fąfara
  Director since October 2019 (Independent)
  Residence: Warsaw, Poland

  Mr. Fąfara was appointed Chief Executive Officer of Helix Immuno-Oncology S.A. in June of 2020. He has over 30 years of financial institution and industrial sector experience where he steered organizational strategy and built successful teams within diverse businesses. Mr. Fafara has held senior executive roles in organizations such as Bank Gospodarstwa Krajowego and Polish Social Insurance Institution. He also possesses experience in working on various board of directors and supervisory boards of, among others, as General Director at ORLEN Lietuva, member of the Supervisory Board PKO BP S.A., Grupa LOTOS S.A., the National Health Fund of Poland, and member of the Supervisory Board of Rockbridge Towarzystwo Funduszy Inwestycyjnych S.A.. Mr. Fafara graduated from Cracow University of Economics in the field of International Economic Relations.

- Artur Gabor
  Director since February 2019 (Independent**)**
  Residence: Konstancin-Jeziorna, Poland

  Artur Gabor founded Gabor & Gabor. Mr. Gabor is a Supervisory Board member of Idea Bank S.A. and Orlen S.A.. He has previously served as a Member of the Polish Institute of Directors, Partner at Warszawska Grupa

Konsultingowa Sp. zoo, Chairman-Supervisory Board at GETIN Bank SA, Director-Financial Sector at IBM Polska Sp zoo, Managing Director-Poland at Crédit Lyonnais Investment Banking Group, Director-Merger & Acquisition at General Electric Capital SNC, Head-Market Development Department at Paged SA and Member of American Chamber of Commerce in Poland. He received an undergraduate degree from University College London and a graduate degree from the University of Warsaw.

- Heman Chao
  Director (Non-Independent), Chief Executive Officer and Chief Scientific Officer
  Residence: Aurora, Ontario, Canada

  Heman Chao, Ph.D. acted as CEO from March 31, 2017, to August 31, 2021. Additionally, he was the Company's Chief Scientific Officer from December 2008 to August 31, 2021. Mr. Chao has been a member of Helix Immuno-Oncology S.A.'s Supervisory Board since January 31, 2018. He is a biochemist with expertise in proteomics technologies. Previously, he was President of Sensium Technologies Inc., a Company subsidiary, between November 2004 and April 2008, when it was amalgamated into the Company. Mr. Chao was previously Vice President of Technology and later Vice President of Research for the Company, between June 2002 to 2004. Between 1999 and June 2002, he was Manager of Sensium Technologies Inc. Prior to joining the Company, he was a research fellow in the federally funded Protein Engineering Network of Centres of Excellence coordinating multi-center research. Dr. Chao received his Ph.D in Biochemistry from Queen's University, Canada in 1994.

  On June 30, 2021, Mr. Chao notified the Board of his intention to step down from the position of CEO, Chief Scientific Officer and member of the Board effective September 1, 2021. As of September 1, 2021, Mr. Chao assumed the position of Chair of the Company's Scientific Advisory Board.

- Krzysztof Saczek
  Director since August 2021 (Independent)
  Residence: Regina, Saskatchewan, Canada

  Dr. Saczek is a Paediatric Surgeon, experienced in treating solid tumors, including malignancies in children. He has trained and practiced in several prominent medical centers in North America, Europe and South Africa. His area of expertise includes gastro-intestinal oncology. Dr. Saczek's professional designations include being a member of the Saskatchewan Medical Association and the CPSS (College of Physicians and Surgeons of Saskatchewan). Currently, Dr. Saczek is the Head of Paediatric Surgery Department at the Regina General Hospital in Regina, Saskatchewan.

- Frank Michalargias
  Chief Financial Officer
  Residence: Richmond Hill, Ontario, Canada

  Photios (Frank) Michalargias, CPA, CA, has been Chief Financial Officer of the Company since June 2005. He possesses over 20 years of senior management experience in both public and private industry; and is experienced in transition and growth management, strategic planning and the raising of debt and equity financing. From 2004 to mid-2005, he was Chief Financial Officer of AP Plasman Corporation, a tier one North American automotive parts supplier controlled by Schroder Ventures International. From 2002 through to mid-2004, he was Senior Finance Director for CFM Corporation, a public company listed on the TSX. Mr. Michalargias' previous tenures include senior financial roles with Trailmobile Corporation, Huhtamaki Oyi and Unilever. He holds a Commerce and Economics degree from the University of Toronto and is a Chartered Professional Accountant, Chartered Accountant. Mr. Michalargias' business functions, as Chief Financial Officer, include financial administration; responsibility for accounting and financial statements; liaising with auditors, the financial community and shareholders; and coordination of expenses/tax activities of the Company.

To the best of the Company's knowledge, the number and percentage of issued Common Shares beneficially owned, directly or indirectly, by the Directors and Officers of the Company, as a group and individually, as at the date of this AIF are as set out in the following table. The table excludes and stock options or warrants beneficially owned, directly or indirectly by the Directors and Officers of the Company, as a group and individually.

Name	Number of Common Shares Held	Percentage of Class[(1)]
Slawomir Majewski	1,705,700	1.20%
Ireneusz Fąfara	0	0.00%
Artur Gabor	0	0.00%
Heman Chao	0	0.00%
Photios (Frank) Michalargias	0	0.00%

Name	Number of Common Shares Held	Percentage of Class[(1)]
Krzysztof Saczek	0	0.00%
Total Common Shares	**1,705,700**	**1.20%**

(1) Based on 142,471,169 Common Shares issued and outstanding as at the date of this AIF.

Cease Trade Orders, Bankruptcies, Penalties and Sanctions

To the knowledge of the directors and officers of the Company:

a) no director or officer of the Company is, as at the date of this AIF or has been, within the 10 years before the date of the AIF, a director or executive officer of any company (including the Company) that:

   (i) while such person was acting in such capacity, was the subject of a cease trade or an order similar to a cease trade order or an order that denied the relevant company access to any exemption under securities legislation, that was in effect for a period of more than 30 consecutive days (an "order"); or

   (ii) was subject to an order that was issued after such person ceased to act in such capacity and which resulted from an event that occurred while such person was acting in such capacity; or

b) no director or officer of the Company or a shareholder holding a sufficient number of securities of the Company to affect materially the control of the Company is, at the date of this AIF or has been, within the 10 years before the date of the AIF, a director or executive officer of any company (including the Company) that:

   (i) while such person was acting in such capacity or with a year of such person ceasing to act in such capacity, became bankrupt, made a proposal under any legislation relating to bankruptcy or insolvency or was subject to or instituted any proceedings, arrangement or compromise with creditors or had a receiver, receiver manager or trustee appointed to hold its assets; or

   (ii) has, within the 10 years before the date of this AIF, become bankrupt, made a proposal under any legislation relating to bankruptcy or insolvency, or become subject to or instituted any proceedings, arrangement or compromise with creditors, or had a receiver, receiver manager or trustee appointed to hold such person's assets.

To the knowledge of the directors and officers of the Company, no director or officer of the company: (a) has been subject to any penalties or sanctions imposed by a court relating to Canadian securities legislation or by a Canadian securities regulatory authority or has entered into a settlement agreement with a Canadian securities regulatory authority, or (b) has been subject to any other penalties or sanctions imposed by a court or regulatory body that would likely be considered important to a reasonable investor in making an investment decision.

INTEREST OF MANAGEMENT AND OTHERS IN MATERIAL TRANSACTIONS

To the Company's knowledge, none of its directors, executive officers, or other insiders, nor any associate or affiliate of any of them, has any material interest, direct or indirect, in any transaction within the three most recently completed financial years or during the current financial year that has materially affected or will materially affect the Company.

TRANSFER AGENT AND REGISTRAR

The Company's transfer agent and registrar for its Common Shares is:

Computershare Trust Company of Canada
100 University Avenue
Toronto, Ontario, Canada, M5J 2Y1

MATERIAL CONTRACTS

The following are the material contracts outside the ordinary course of business entered into by the Company which are still in effect:

1) Technology License Agreement with the NRC dated April 28, 2005 and amendment dated December 2, 2009.

The Company entered into a worldwide exclusive license with the NRC, through which it obtained the right to combine an antibody that specifically binds to lung adenocarcinoma cells with minimal cross reactivity to other tissues with the Company's DOS47™ technology. Unless earlier terminated pursuant to the license agreement, the license terminates when the last patent right related to the licensed technology expires, on a country-by-country basis. The Company is required to pay a royalty of 3% of net sales, with a minimum royalty of $10,000 per year. The Company is also required to make certain milestone payments as follows: $25,000 upon successful completion of Phase I clinical trials; $50,000 upon successful completion of phase IIb clinical trials; $125,000 upon successful completion of phase III clinical trials; and $200,000 upon receipt of market approval by a regulatory authority. L-DOS47 is subject to this agreement.

2) The Company in-licensed the worldwide rights for anti-CEACAM6 single domain antibody 2A3 from the NRC. Pursuant to a collaboration and licensing agreement dated February 20, 2017 with the NRC, the Company is required to pay a royalty of 3% of net sales, with a minimum royalty of $10,000 per annum generated from the use of a certain antibody to target cancerous tissues of the lung. In addition to the royalty payments, the Company is also required to make certain milestone payments for the first licensed product: $25,000 upon successful completion of Phase I clinical trials; $50,000 upon successful completion of Phase IIb clinical trials; $150,000 upon successful completion of Phase III clinical trials; $200,000 upon receipt of first regulatory approval by a regulatory authority; and $200,000 upon receipt of a second regulatory approval by a regulatory authority. For the development of each subsequent licensed product: $200,000 upon receipt of first regulatory approval by a regulatory authority; and $200,000 upon receipt of a second regulatory approval by a regulatory authority. As it relates to sub-licensing arrangement, the Company is required to pay the NRC 33% of any sub-licensing revenues received.

3) Pursuant to the Company's collaboration and licensing agreement dated February 20, 2017 with the NRC, the Company granted a sublicense to limited rights over to HIO for the worldwide territory except Canada.

    a) HIO will pay the amounts of the milestones called for in the collaboration and licensing agreement between the Company and the NRC increased by 20% for each drug product.
        i. The amount corresponding to the collaboration and licensing agreement shall be paid directly to the NRC by HIO.
        ii. The remaining 20% shall be paid directly to the Company by HIO.

    b) HIO will pay a 3% royalty on sales revenue for all product sales and services directly to the NRC.
    c) HIO will pay a 1% royalty on sales revenue for all product sales and services directly to the Company.

4) The Company signed a collaboration and licensing agreement on March 16, 2018 with ProMab to develop novel antibody and CAR-T for particular hematological malignancies. Under the collaboration agreement, Helix retains commercial rights for Canada and Europe (except Russia).

    a) The Company will pay the following royalties to ProMab:
        i. 5% of annual aggregate net sales up to USD$250,000
        ii. 6% of annual aggregate net sales above USD$250,000

    b) The Company will pay the following milestone to ProMab:
        i. USD$1,000,000 upon the completion of Phase I clinical study meeting primary objectives of the trial for each drug product; and
        ii. USD$5,000,000 upon first commercial sale of each drug product.

5) Pursuant to the Company's collaboration agreement dated March 16, 2018 with ProMab, the Company granted a sublicense to HIO for Europe (except Russia).

    a) HIO will directly pay to ProMab the following milestone payments:
        i. USD$1,000,000 upon the completion of Phase I clinical study meeting primary objectives of the trial for each drug product; and
        ii. USD$5,000,000 upon first commercial sale of each drug product.

    b) HIO will pay the Company the following milestone payments
        i. USD$250,000 as a single milestone payment at the time of the first commercial sale in the HIO territory of a each drug product that uses or embodies the technology;

    c) HIO will directly pay to ProMab the e following royalties
        i. 5% of annual aggregate net sales up to USD$250,000
        ii. 6% of annual aggregate net sales above USD$250,000

    d) HIO will directly pay to the Company the following royalties

i. 2% of annual aggregate net sales up to USD$250,000
ii. 2% of annual aggregate net sales above USD$250,000

6) The Company 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. Under the terms of the agreement dated November 18, 2016, Xisle paid an up-front fee of USD$125,000 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.

   a) Milestones as follows:
      i. USD$3,000,000 upon initiation of the first Phase 3 trial anywhere in Xisle's territory;
      ii. USD$5,000,000 upon first submission of New Drug Application or similar for approval in the Xisle territory; and
      iii. USD$10,000,000 upon first commercial sale of a product in the Xisle territory.

   b) Royalties as follows until the lapse of 10 years from first commercial sale of a product in Xisle's territory:
      i. 8% on annual net sales up to USD$50,000,000,
      ii. 10% on the next annual net sales of USD$25,000,000, and
      iii. 12.50% on the annual net sales above USD$75,000,000.

7) On May 11, 2021, the Company entered into the Lind Agreement with Lind Global Macro Fund, LP, a New York based institutional investment fund managed by Lind. The Company closed the First Tranche under the Lind Agreement on May 13, 2021 when it issued a Convertible Security with a two year term and a face value of $4,112,500 and an aggregate of 1,957,056 Warrants exercisable into Common Shares for a period of 48 months at an exercise price of CAD$1.0283 per Common Share. The Convertible Security issued under the First Tranche accrues a simple interest rate obligation of 8.75% per annum on the amount funded, being CAD$3.5 million, which interest is prepaid and attributed to the face value of the Convertible Security. The Company also paid Lind a 3% commitment fee on the amount funded under the First Tranche, as well as under any second tranche, which as of the date of this AIF has not yet been completed.

   Each Convertible Security issuable under the Lind Agreement will have a two-year term from the date of issuance and will accrue simple interest rate obligation of 8.75% per annum on the amount funded, which interest shall be prepaid and attributed to the face value of each Convertible Security upon the issuance. Lind is be entitled to convert the Convertible Securities into Common Shares over the term of the applicable Convertible Security, subject to certain limitations, at a conversion price equal to 85% of the five-day trailing volume-weighted average price ("VWAP") of the Common Shares prior to the date a notice of conversion is provided to the Company by Lind. The Lind Agreement includes certain restrictions on the maximum face value of each of the Convertible Securities that may be converted in any particular month. In addition, the Company has the option to buy-back 66.7% of the Convertible Securities in cash at any time with no penalty, subject to the option of Lind to convert up to 1/3 of the face value of the applicable Convertible Security into Common Shares at the time of such buy-back. If the Convertible Security is repaid by the Company within 180 days of issuance, the face value amount owed will be reduced pursuant to the terms of the Lind Agreement. Lind will also be entitled to accelerate its conversion right to the full amount of the face value or demand repayment of the face value in cash upon a default and other designated events as set out in the Lind Agreement. To the extent that the full face value of a Convertible Security has not been converted at the maturity date of the applicable Convertible Security, the outstanding balance of such face value shall be to be repaid to Lind by the Company in cash.

   The LIND Agreement is subject to covenant requirements. In the event of default LIND may declare, by notice to the Company, effective immediately, all outstanding obligations by the Company under the Funding Agreement to be immediately due and payable in immediately available funds and terminate the agreement. No such declaration has been made at time of filing of this AIF.

Electronic copies of the contracts set out above may be accessed under the Company's profile on SEDAR at www.sedar.com.

INTERESTS OF EXPERTS

The Company's auditors for fiscal 2021 are Marcum LLP. 53 State Street, 17th Floor, Boston, MA, 02109, USA. Marcum LLP is independent of the Company in accordance with the applicable rules of professional conduct/code of ethics of The Chartered Professional Accountants of Ontario.

The Company's auditors for fiscal 2020 were BDO Canada LLP. 3115 Harvester Road, Suite 400, Burlington, Ontario, Canada, L7N 3N8. BDO Canada LLP is independent of the Company in accordance with the applicable rules of professional conduct/code of ethics of The Chartered Professional Accountants of Ontario.

AUDIT COMMITTEE DISCLOSURE

Audit Committee Responsibilities

The Company's Audit Committee is responsible for reviewing the Company's financial reporting procedures and internal controls and for the retention and review of the performance of the Company's external auditors, together with reviewing the scope and results of the Company's audits and managing the professional services furnished by the independent auditors. The Audit Committee is also responsible for reviewing the annual and quarterly financial statements and accompanying Management's Discussion and Analysis prior to their approval by the full Board. The Audit Committee also reviews the Company's financial controls with the auditors of the Company on an annual basis.

The Company's independent auditor is accountable to the Board and to the Audit Committee. The Board, through the Audit Committee, has the ultimate responsibility for evaluating the performance of the independent auditor, and through the shareholders, to appoint, for replacing and compensating the independent auditor.

The Company's Audit Committee has a charter, a copy of which is attached as Schedule "A".

Composition and relevant education and experience

The Audit Committee is currently comprised of three members: Artur Gabor, Ireneusz Fąfara and Krzysztof Saczek, all of whom are independent directors. Mr. Artur Gabor was appointed Chair of the Audit Committee on April 15, 2019.

All members of the audit committee are financially literate, meaning they have the ability to read and understand a set of financial statements that present a breadth and level of complexity of accounting issues that are generally comparable to the breadth and complexity of the issues that can reasonably be expected to be raised by the Company's financial statements. A brief description of the education and experience of each of the audit committee members is set under the heading "*Directors and Officers*", above.

Exemptions Relied Upon

None.

Pre-approval of non-audit services

It is the Company's policy that all audit and non-audit services performed by its external auditors will continue to be pre-approved by the Company's Audit Committee.

Auditor fees

The Company appointed Marcum LLP as new auditors for fiscal 2021. For fiscal 2020 the Company's auditors were BDO Canada LLP. The total fees billed for professional services are as follows:

Item	2021		2020	
	Amount	Percentage	Amount	Percentage
Audit-Fees	$126,500	100%	$102,000	93%
Tax Fee	$0	0%	$0	0%
All Other Fees	$0	0%	$8,160	7%
Total	$126,500	100%	$110,160	100%

ADDITIONAL INFORMATION

Additional information, including directors' and officers' remuneration and indebtedness, principal holders of the Company's securities, securities authorized for issuance under equity compensation plans, and interests of insiders in material transactions, if applicable, is contained in the Company's Management Proxy Circular for its most recent annual meeting of shareholders that involved the election of directors.

Management's Discussion and Analysis of Results of Operations and Financial Condition of the Company as at July 31, 2021, as filed on the Company's profile on SEDAR at www.sedar.com, is incorporated by reference herein.

Any request for any documents referred to above should be made to the Chief Financial Officer, attention: Photios Michalargias, 9120 Leslie Street, Suite 205, Richmond Hill, Ontario, L4V 3J9 Canada or by fax to (905) 841-2244.

Additional information relating to the Company can be found under the Company's profile on SEDAR at www.sedar.com and the Company's website at www.helixbiopharma.com.

GLOSSARY

Adenocarcinoma: Cancer that originates in glandular tissue.

Biphasix™ technology: Helix's proprietary platform technology designed for dermal, mucosal, transdermal and transmucosal delivery of molecules.

Board: The board of directors of the Company.

CBCA: means the *Canada Business Corporations Act*.

cGMP: Is an acronym for Current Good Manufacturing Practices, a term that is recognized worldwide for the control and management of manufacturing and quality control testing of foods and pharmaceutical products.

Colposcopy: A medical diagnostic procedure to examine the epithelial cells of the cervix, vagina, and vulva, especially for early signs of cancer.

CTA: Clinical Trial Application.

Dermal: Pertaining to the region of skin to the epidermis, consisting of a dense bed of vascular connective tissue. Dermal administration refers to the delivery of substances or compounds into the dermal region.

Dysplasia: A term used in pathology to refer to an abnormal growth or development of cells, tissue or organs. Dysplasia is often an indicator of early stage neoplasia or the abnormal proliferation of cells.

Epithelial: Of, pertaining to, or characterized by the epithelium, which is tissue, consisting of one or more cellular layers separated by very little intercellular substance, that covers most internal and external surfaces of the body.

FDA: United States Food and Drug Administration. The regulatory agency that oversees the development, manufacture, sale and use of diagnostic and therapeutic medical products in the United States.

GMP: Good Manufacturing Practice.

Health Canada: The department of the federal government of Canada that is responsible for all health-related matters in Canada on a national level.

HIO: Helix Immuno-Oncology S.A..

Histological: Of, pertaining to, or characterized by histology, which is the branch of biology dealing with the study of tissues, cells and their structure, especially at the microscopic level.

HPV: Human Papilloma Virus. One of the most common sexually transmitted infections, causing cervical dysplasia and ano-genital warts as well as being linked to a variety of cancers.

IFRS: International Financial Reporting Standards issued by the International Accounting Standards Board, and as adopted by the Chartered Professional Accountants Canada.

Immunoconjugate: A molecular complex consisting of one or more antibodies linked to a second compound.

IND: Investigational New Drug.

Intraepithelial: Occurring in or among cells of the epithelium including the cells of the epithelial layer of the skin.

Lipid: Fats or fat-like substances characterized by being water-insoluble.

Low-grade cervical lesions: For the purposes of this AIF, this term refers to cervical abnormalities combining an LSIL finding on Pap smear and a CIN1 or CIN2 diagnosis on colposcopy.

LSIL: Low-grade Squamous Intraepithelial Lesions.

Neoplasia: A pathological process that results in the abnormal and often uncontrolled growth and proliferation of cells, and is usually associated with cancer.

NRC: National Research Council of Canada.
NSCLC: Non-small cell lung cancer.

Pharmacokinetic: The action of drugs in the body over a period of time, including the processes of absorption, distribution, localization in tissues, biotransformation (metabolism) and excretion.

Phase I clinical trials: Clinical trials used to assess the potential toxicity of a new drug, primarily involving healthy volunteers, under the regulations of the applicable jurisdiction.

Phase II clinical trials: Clinical trials used to assess the effectiveness and most effective dosage of a new drug under the regulations of the applicable jurisdiction.

Phase III clinical trials: Late stage clinical trials used to assess a drug for efficacy and safety at several independent sites in a large number of patients under the regulations of the applicable jurisdiction.

PNCRD: Polish National Centre for Research and Development.

RECIST: Response Evaluation Criteria In Solid Tumors. A set of published rules that define when cancer patients improve, stay the same, or worsen during treatments.

ProMab: A biotechnology company that develops and commercializes recombinant proteins, custom monoclonal antibodies, CAR-T products through the integration of bioinformatics, gene cloning, protein expression and purification, and immunology, using novel high-throughput technologies.

Therapeutic: A medical treatment or curative product for a disease.

Topical Interferon Alpha-2b: A topical preparation under development by the Company that is intended to be self-applied to HPV-infected tissues, in order to deliver interferon-alpha intradermally. It is based on Helix's proprietary Biphasix™ drug delivery technology.

TSX: The Toronto Stock Exchange.

Transdermal: Access to the systemic blood circulation via migratory passage through the multiple layers of skin.

Transmucosal: Access to the systemic blood circulation via migratory passage through the multiple layers of mucosa.

SCHEDULE A
AUDIT COMMITTEE CHARTER

HELIX BIOPHARMA CORP.

The Audit Committee of the Board of Directors (the "Board") of Helix BioPharma Corp. (the "Corporation") shall have the composition, responsibilities, powers, duties and authority specified in this Charter.

I. Purpose

The Audit Committee's purpose is to:

a. Assist the Board's oversight of:

i. The integrity of the Corporation's financial statements;

ii. The Corporation's financial accounting and reporting, the system of internal controls established by management, and the adequacy of internal and independent auditing relative to these activities;

iii. The Corporation's compliance with legal and regulatory requirements; and

iv. The qualifications, independence and performance of the independent public accounting firm auditing the Corporation's financial statements.

b. Prepare such reports as may be required from time to time by applicable securities laws and by the rules and regulations of applicable regulatory authorities (including any stock exchange on which the Corporation's securities are listed) (such laws, rules and regulations being hereinafter referred to, collectively, as the "Rules and Regulations").

c. Oversee the work of the Corporation's independent accounting firm, including the resolution of disagreements between management and the independent public accounting firm regarding financial reporting.

II. Composition, Appointment and Procedures.

a. The Audit Committee shall consist of at least three members of the Board, each of whom shall be, subject to such exceptions as may be permitted by the Rules and Regulations, an "independent director" and "financially literate" within the meaning of the Rules and Regulations.

b. No member of the Audit Committee may concurrently serve on the audit committee of more than two other public companies unless the Board determines that such simultaneous service would not impair the ability of such director to effectively serve on the Audit Committee.

c. The members of the Audit Committee shall be appointed by the Board and shall continue to act until their successors are appointed. Members shall be subject to removal at any time by the Board.

d. The Audit Committee shall meet at least four times each year. At such meetings, the Audit Committee shall discuss such audit matters as the Audit Committee deems appropriate with the Corporation's CFO and independent public accounting firm.

e. Periodically, the Audit Committee shall meet separately with the independent public accounting firm.

III. Duties and Responsibilities with Respect to Audit, Accounting and Financial Disclosure.

The Audit Committee shall:

a. Prior to filing with the applicable regulatory authorities or otherwise publicly disclosing the information, review and discuss with the Corporation's management and independent public accounting firm:

i. the Corporation's annual audited financial statements, quarterly financial statements, and annual and quarterly financial press release, including the Corporation's disclosures under “Management's Discussion and Analysis”; and,

ii. the scope and results of the annual audit, or any interim reporting;

b. Review and discuss with the Corporation's management and independent public accounting firm:

i. major issues regarding accounting principles and financial statement presentations, including any significant changes in the Corporation's selection or application of accounting principles, and major issues as to the adequacy of the Corporation's internal controls and any special audit steps adopted in light of material control deficiencies;

ii. analyses prepared by management and/or the independent public accounting firm setting forth significant financial reporting issues and judgments made in connection with the preparation of the financial statements, including analyses of the effects of alternative IFRS methods on the financial statements;

iii. the effect of regulatory and accounting initiatives, as well as off-balance-sheet structures, on the Corporation's financial statements; and

iv. the type and presentation of information to be included in quarterly and annual financial press releases;

c. Review with the Corporation's independent public accounting firm any audit problems or difficulties and management's response, including:

i. any restrictions on the scope of the activities of the independent public accounting firm;

ii. any restriction on the independent public accounting firm's access to requested materials;

iii. any significant disagreements with management; and

iv. any material audit differences that the independent public accounting firm noted or proposed but for which the Corporation's financial statements were not adjusted;

d. Resolve any disagreements between the independent public accounting firm and Corporation's management regarding financial reporting;

e. Discuss with the Corporation's management, independent public accounting firm and Chief Financial Officer the adequacy of the Corporation's internal accounting, financial and operating controls;

f. Be satisfied that adequate procedures are in place for the review of the Corporation’s public disclosure of financial information extracted or derived from the Corporation’s financial statements, and periodically assess the adequacy of such procedures; and

g. Report to the Board with respect to the foregoing.

IV. Specific Responsibilities with Respect to the Corporation’s Independent Public Accounting Firm

The Corporation's independent public accounting firm is ultimately accountable to the Board and shall report directly to the Audit Committee.

a. The Audit Committee shall recommend to the Board:

i. The independent public accounting firm to be nominated for the purpose of preparing or issuing an auditor's report or performing other audit, review or attest services for the Corporation; and

ii. The compensation of the independent public accounting firm.

b. The Audit Committee shall annually evaluate the qualifications, performance and independence of the independent public accounting firm and the lead partner.

c. The Audit Committee shall pre-approve all non-audit services to be provided to the Corporation or its subsidiary entities by the Corporation's independent public accounting firm.

d. The Audit Committee shall review and approve the compensation and terms of engagement of the Corporation's independent public accounting firm before the firm provides any audit, audit-related, tax or permitted non-audit services.

e. At least annually, the Audit Committee shall obtain and review a report by the independent public accounting firm describing:

i. the firm's internal quality control procedures,

ii. any material issues raised by the firm's most recent internal quality control review or peer review; and

iii. all relationships between the firm and the Corporation.

f. At least annually, the Audit Committee shall obtain from the independent public accounting firm assurance that they are not aware of any illegal act that has or may have occurred.

g. The Audit Committee shall report to the Board with respect to the foregoing.

V. Additional Powers, Duties and Authority.

The Audit Committee shall have additional powers, duties and authority to:

a. Monitor, review, and, if necessary or advisable, revise and update the Corporation's procedures for:

i. the receipt, retention and treatment of complaints received by the Corporation regarding accounting, internal accounting controls and auditing matters; and

ii. the confidential, anonymous submission by the Corporation's employees of concerns regarding accounting or auditing matters;

b. Discuss with the Corporation's management the Corporation's guidelines and policies with respect to risk assessment and risk management, including the Corporation's major financial risk exposures and the steps management takes to monitor and control such exposures;

c. Annually review the Audit Committee's performance and Charter, which shall include evaluating each member's qualifications, attendance, understanding of the Audit Committee's responsibilities and contribution to the functioning of the Audit Committee, and recommend any proposed changes to the Board for approval;

d. Prepare such reports as are required by the Rules and Regulations;

e. Review with the Corporation's legal counsel any legal matters that may have a material impact on the financial statements, the Corporation's Code of Business Conduct and Ethics and any material reports or inquiries received from regulators or governmental agencies;

f. As the Audit Committee may deem appropriate, retain and terminate any legal, accounting or other consultants, who shall report directly to the Audit Committee, on such terms and conditions, including fees, as the Audit Committee in its sole discretion shall approve;

g. Request that any of the Corporation's officers, employees, outside counsel or independent public accounting firm attend any meeting of the Audit Committee or meet with any of the Audit Committee's members or consultants;

h. Review and approve the Corporation's hiring policies regarding partners, employees and former partners and employees of the Corporation's present and former independent public accounting firm; and

i. Report to the Board with respect to the foregoing.